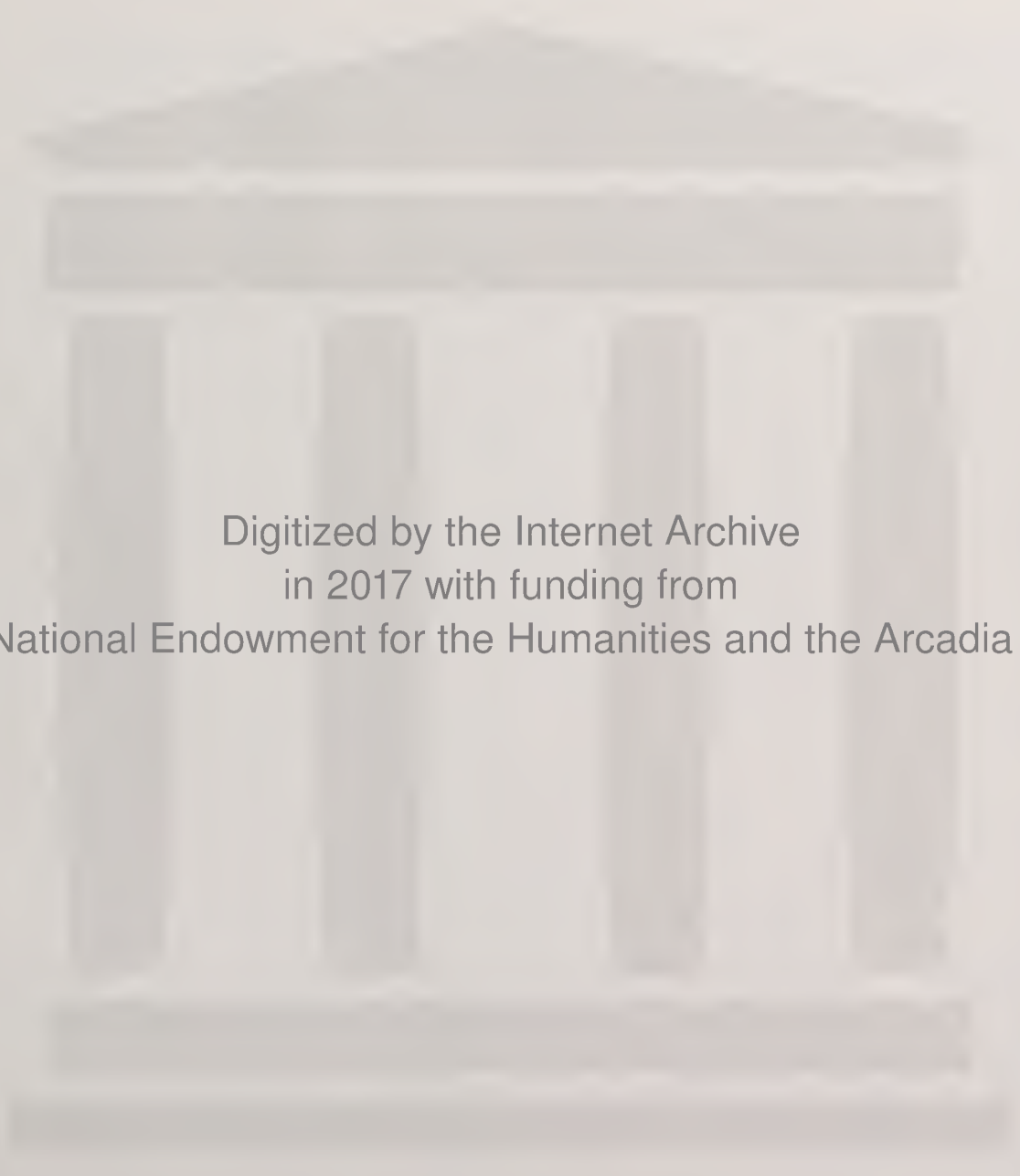




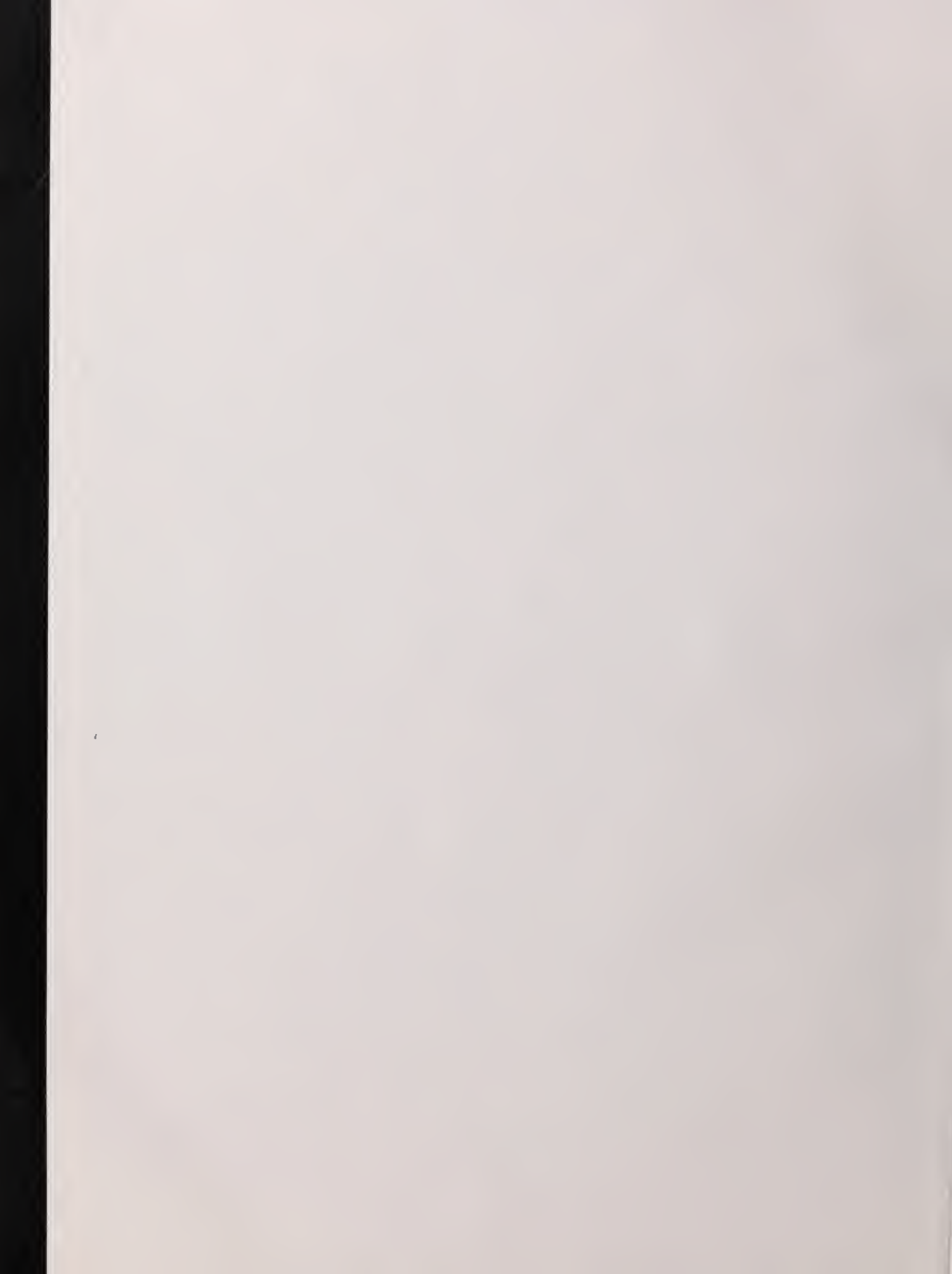
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# Columna del Editor



Comenzamos el año con una gran satisfacción: la de tener nuestra revista circulando en el mes que le corresponde. Es la primera vez en muchos años que esto se consigue y la Junta Editora se siente muy orgullosa de haberlo logrado pues fue producto de mucho esfuerzo. Confiamos que esto pueda continuar durante este año ya que se ha establecido una eficiente coordinación de trabajo con la imprenta lo que permite la circulación de la revista cada cuatro semanas. Sin embargo la puntualidad en la circulación, que a su vez permitiría más ingresos por la consecución de anunciantes nuevos, se vé algo incierta al presente por la escasez de material científico que se viene recibiendo. En los momentos que escribimos estas líneas (12/28/82) contamos con sólo 50% del material necesario para completar el número correspondiente al mes de febrero de 1983, el cual debe estar en la imprenta en las próximas dos semanas para asegurar su circulación en ese mes. La razón de esta situación escapa a nuestro entendimiento pues la revista se ha mejorado gráficamente haciéndola más atractiva y estimulante a la lectura. Los miembros de la Junta Editora de quienes se esperaba aportación de material científico así lo han hecho. Se le ha comunicado personalmente, y en otras ocasiones se les han escrito cartas a Jefes de Departamento y Directores de Educación Médica de instituciones de enseñanza médica locales exhortándolos a que viertan su experiencia clínica o de investigación en nuestro Boletín.

La circulación de la revista por las bibliotecas de las principales Escuelas de Medicina de Norte, Centro y Sur América al igual que algunas en Europa y en Asia le otorgarían una dimensión internacional a nuestros investigadores jóvenes a la vez que contribuiría a la difusión de la cultura médica nacional, una de las razones de ser de nuestro Boletín. Si esta tendencia persiste y no se reciben manuscritos en la cantidad y calidad necesaria la Junta Editora del Boletín de la Asociación Médica de Puerto Rico tendrá que recomendar a la Junta de Directores los cambios que estime pertinentes para asegurar la circulación periódica de nuestro órgano oficial sin que se convierta en un lastre económico.

Incluimos en esta edición el Índice de Materias del Volumen 74 (1982) del Boletín el cual por error involuntario se publicó incompleto en el mes de diciembre.

En este número se presenta un estudio muy importante sobre la mamografía, se editorializa sobre este tema, y se publican las indicaciones y recomendaciones actuales para esta prueba diagnóstica. Otros estudios clínicos incluyen experiencias locales sobre Melanoma Maligno y sobre la Estenosis Pilórica a la vez que el Dr. Toledo-Pereyra contribuye desde Detroit, Michigan con otro de sus estudios sobre transplante de órganos. Todos estos trabajos originales junto al artículo de repaso sobre Hepatitis Viral y las secciones fijas de nuestro Boletín hacen que este primer número de 1983 sea de gran interés, tanto por la calidad científica de su contenido como por la diversidad del mismo.

**Rafael Villavicencio, MD**  
Presidente Junta Editora  
Boletín Asociación Médica de Puerto Rico



ASOCIACION MEDICA DE PUERTO RICO

# BOLETIN



VOL. 75/NUM. 1

ENERO 1983

## NUESTRA PORTADA:

Los Tres Reyes Magos. Cartel por el artista puertorriqueño Antonio (Tony) Maldonado. Este cartel originalmente anunciaba los programas navideños que se iban a llevar a cabo en las diferentes comunidades de la Isla auspiciados por la División de Educación a la Comunidad del Departamento de Instrucción Pública. Más tarde se utilizó por la UNICEF en una postal de Navidad como contribución al Fondo de las Naciones Unidas para la Infancia.

Tony nació en el sector de Palo Alto del barrio Coto Sur de Manatí en el año 1920. De muy niño su afición por el dibujo era grande, copiaba todo lo que caía en sus manos, fotos de periódicos, ilustraciones de libros, estampas religiosas, etc. Mientras cursaba el sexto grado en la Escuela José Severo Quiñones su maestra de español, doña Magda López de Victoria, vista su afición por el dibujo, lo incluyó en las clases de dibujo que daba en su casa luego de las horas escolares. Al terminar el curso de arte fue galardonado con el primer premio de la clase, consistente en una caja de pinturas de agua con las que se inició en la brega del color.

En 1936 ingresa al taller del maestro Juan A. Rosado en Puerta de Tierra, donde estudia dibujo por algún tiempo. Por varios años permanecerá aquí pintando rótulos, mientras hace sus estudios de Escuela Superior en la Escuela Nocturna Labra. Sigue las prácticas del dibujo con el maestro Sánchez Felipe, de pintura con Gretchen Wood y en la Universidad de Puerto Rico asiste como oyente a las clases de dibujo y pintura de don Cristóbal Ruiz. Marcha en el 1947 a Mejico para ingresar en la Escuela Nacional de Artes Plásticas donde permanece por tres años.

De nuevo en Puerto Rico trabaja por algunos años en el taller del maestro Rosado. En Manatí labora por algún tiempo como escultor en la fábrica de figuras para Nacimientos Miller. En los inicios de la televisión en Puerto Rico laboró como escenógrafo en Telemundo. En 1957 trabaja en el taller de artes gráficas de la División de Educación de la Comunidad, donde aun permanece.

Desde sus inicios como pintor su predilección por la acuarela es manifiesta. Tal vez por las propiedades de este medio para fijar la atmósfera cambiante del paisaje de nuestra tierra. También ha hecho trabajos al temple y al óleo, varios retratos, algunos murales, grabados, etc. En la División ha realizado numerosas ilustraciones para libros, e infinidad de carteles para películas y actividades del programa, así como para otras agencias y entidades interesadas. También ha realizado escenografías para el teatro Tapia y otros teatros del país.

Su primera exposición fue precisamente de acuarelas en el 1941 en el Ateneo Puertorriqueño y desde entonces su obra ha figurado en numerosas exposiciones colectivas en nuestro país y el exterior.

La reproducción de la obra en nuestra portada ha sido posible gracias a la cooperación del autor con nuestra Asociación. Le damos las gracias a Tony Maldonado.

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# EDITORIAL



## MAMOGRAFIA 1983

El cáncer de seno en Puerto Rico constituye la primera causa de muerte por malignidad en nuestra mujeres y la primera causa de muerte por cualquier razón en las mujeres entre los 40 y los 49 años. Es alarmante observar el desmesurado aumento en la incidencia de esta malignidad desde una tasa ajustada de 9.9 por 100,000 habitantes en el 1950, a una tasa ajustada de 24.1 en el 1980 (tasas crudas de 9.9 a 34.1 en este mismo período). Y si alarmante es ver que 556 mujeres fueron diagnosticadas de este mal en P.R. durante el 1980, mas alarmante aún es ver que la tasa de mortalidad durante estos pasados 30 años ha ido de 3.8 en el 1950 a 5.8 en el 1980, habiéndose mantenido cerca de este más reciente nivel durante la pasada década.\*

La cirugía más o menos agresiva, la radioterapia, y la quimioterapia o las combinaciones de estas no han podido mejorar sustancialmente este deprimente cuadro. Durante los pasados 10 años innumerables estudios han llevado a la conclusión de que el diagnóstico temprano de esta enfermedad constituye el único factor que ha logrado reducir la morbilidad y la mortalidad en este cáncer. Es hacia ese diagnóstico temprano que debemos dirigir nuestros mayores esfuerzos.

Gracias a los excelentes estudios realizados por el Colegio Americano de Radiología, la Sociedad Americana del Cáncer, y El Instituto Nacional del Cáncer entre otros, la Mamografía ha quedado establecida como la modalidad diagnóstica más sensitiva y específica para lograr el diagnóstico temprano del cáncer de seno. Unida al autoexamen y al reconocimiento por un médico diestro en el examen clínico de los senos, la mamografía ofrece hoy por hoy el mejor potencial de descubrir lesiones en estadios sumamente tempranos con pronósticos de curabilidad que sobrepasan el 90%.

Cuando hablamos de mamografía para descubrir lesiones malignas tempranas en los senos, tenemos que insistir en que nos referimos al estudio radiográfico de los senos con un equipo utilizado y diseñado específicamente para este estudio en particular, e interpretado por un radiólogo debidamente adiestrado y al día en esta modalidad. Nos satisface saber que el número de equipos de esta naturaleza adquiridos por radiólogos en diversos puntos de Puerto Rico durante estos pasados 2 años, ha aumentado considerablemente. Igual-

mente nos complace haber establecido en agosto de 1980 una facilidad mamográfica en el Hospital Universitario en torno a la cual se ha desarrollado un programa de entrenamiento para tecnólogos y residentes de Radiología en esta disciplina. Es muy temprano aún para ver los frutos de estas personas y estos equipos en la Isla. Si los radiólogos que poseen estos equipos tienen o adquieren el entrenamiento y la experiencia necesaria, veremos en los próximos años una dramática reducción en la mortalidad y en la morbilidad por cáncer de mama en Puerto Rico.

Es desafortunado que objeciones con una base cuestionable científica produjeron un clima de histeria hace unos años en cuanto al uso de la mamografía en el estudio de mujeres asintomáticas. Conjeturas altamente exageradas y ya desmentidas o puestas en adecuada perspectiva científicamente, evitaron que muchas mujeres sintomáticas retardaran, con consecuencias funestas, su diagnóstico de cáncer de mama. Si se siguen las recomendaciones del Colegio Americano de Radiología\*\* en cuanto a los estudios mamográficos, no debe haber reservas ni temores para someter a un paciente a este examen siempre y cuando se realice el mismo con un equipo especializado para esta prueba, y bajo la supervisión de un radiólogo con adiestramiento y experiencia en mamografía. De estar indicada una mamografía de acuerdo a estos criterios, el riesgo real estaría en rechazar este estudio.

\* Cáncer en Puerto Rico - Registro Central del Cáncer - 1980 (en imprenta al presente).

\*\* American College of Radiology, Guidelines for Mamography (pag.24).

Bernardo J. Marques, MD  
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Centro Médico de Puerto Rico

# ESTUDIOS CLINICOS

## Mamografía: Experiencia en el Hospital Universitario

Bernardo J. Marqués, M.D.

El cáncer de seno en Puerto Rico ha sostenido un alarmante ritmo ascendente en su incidencia durante los pasados 30 años. En el 1980, 556 mujeres en el país fueron diagnosticadas como nuevos casos de esta malignidad.<sup>1</sup>

El diagnóstico temprano del cáncer de seno ha probado ser el factor más importante en reducir la mortalidad y la morbilidad en esta enfermedad.<sup>2 3 4</sup> Aún cuando los más prometedores resultados se obtienen en el estudio de grandes poblaciones de mujeres asintomáticas sobre los 40 años<sup>2 3 4</sup> es innegable el valor de la mamografía en la evaluación de mujeres sintomáticas, en las cuales la incidencia de malignidad es mayor, y el diagnóstico clínico difícil.

La División de Mamografía del CMPR se creó en Agosto de 1980 con la instalación de una unidad radiográfica dedicada y diseñada específicamente para este estudio, en el Hosp. Universitario. Desde su instalación hasta abril de 1982 más de 4,000 mujeres han sido estudiadas en esta facilidad.

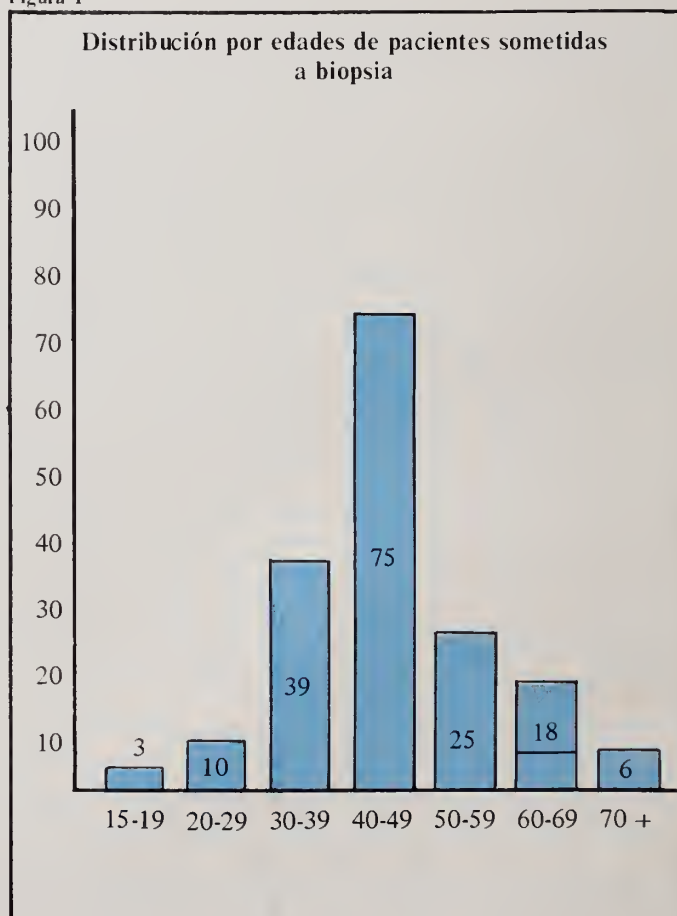
El presente estudio analiza nuestra experiencia con las 1200 mujeres referidas a nuestra División por la Clínica de Enfermedades del Seno del Hospital Universitario, durante este período de tiempo. Hemos seleccionado esta clínica para nuestro análisis por sobre nuestras otras fuentes de referido, dado el "expertise" de los cirujanos envueltos en ella,<sup>5</sup> y el interés y cooperación extraordinario del personal de enfermería de dicha clínica,<sup>6</sup> en el seguimiento y manejo rápido de estas pacientes.

### Materiales y Métodos

Mil docientas mujeres entre las edades de 16 a 90 años fueron referidas para mamografía entre agosto de 1980 y abril de 1982 como parte de su evaluación en la Clínica de Enfermedades del Seno a la que habían sido referidas por síntomas o signos de enfermedad de la mama. Ciento ochenta y tres de estas pacientes (15%) fueron sometidas a biopsia debido a sus hallazgos clínicos y/o mamográficos. En 45 de ellas (25%) se estableció el diagnóstico de malignidad mientras que en 138 de ellas (75%) enfermedad benigna o ausencia de enfermedad fue documentada. Tres de los

pacientes con carcinoma y 4 con lesiones benignas tuvieron que ser omitidos de este estudio por no ser posible localizar la mamografía y el expediente clínico de las mismas. Los restantes 176 pacientes con prueba patológica (Fig. 1) constituyen el sujeto de este estudio, a saber, 42 con enfermedad maligna y 134 con enfermedad benigna.

Figura 1



### Enfermedad Fibroquística

De los 134 casos con patología benigna, 110 fueron catalogados patológicamente como enfermedad fibroquística (Fig. 2). Nueve de los casos con enfermedad fibroquística tenían elementos de papilomatosis intraductal, una condición considerada como premaligna. La consideración de la papilomatosis intraductal como una lesión premaligna fue justificada en nuestros 9 casos. Dos de estas pacientes habían sufrido ya mastectomía unilateral por carcinoma previo y una de estas 2 presentó un carcinoma en el seno

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remanente en el momento de nuestro estudio. Otra de estas 9 pacientes en la cual el diagnóstico de papilomatosis intraductal se había establecido 3 años antes, padecía al momento de nuestro estudio de un carcinoma de mama. Los hallazgos mamográficos en otra de estas 9 pacientes eran altamente sospechosos de malignidad (microcalcificaciones) pero esto no fue confirmado patológicamente, mientras que otra de estas pacientes tenía 2 hermanas con carcinoma de mama. Las edades de estas pacientes fluctuaron entre los 41 y los 72 años. Desafortunadamente no encontramos hallazgos mamográficos característicos o específicos de papilomatosis intraductal en estos casos y la apariencia mamográfica de los mismos fue la de una displasia no específica. El cuidadoso y frecuente seguimiento clínico y mamográfico en pacientes en las cuales se ha establecido el diagnóstico de papilomatosis intraductal es extremadamente importante. La mastectomía profiláctica que se realiza en muchos de estos casos en centros de los E.E. U.U., podría considerarse en ellos.

Figura 2

### ENFERMEDAD FIBROQUISTICA (110)

EFQ sin cualificar o sin otra patología - 55  
EFQ cualificada o con otra patología - 55

Mazoplasia .....	6
Adenosis esclerosante .....	7
Ectasia ductal .....	4
Papilomatosis intraductal .....	9
Mastitis crónica o aguda .....	3
EFQ bilateral .....	6
Papiloma intraductal .....	3
Adenolipoma .....	3
Necrosis de grasa .....	1
Fibroadenoma .....	4
Carcinoma .....	13

### Fibroadenomas

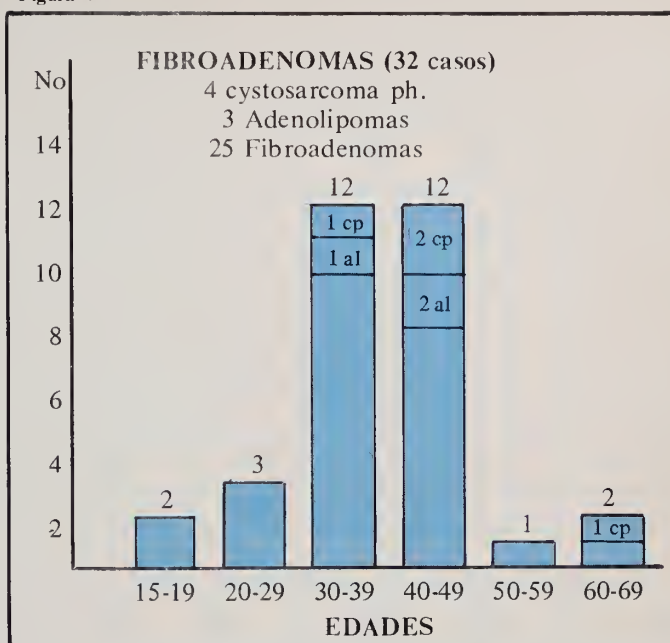
En 20 de los 32 pacientes con diagnóstico patológico de fibroadenomas el diagnóstico mamográfico ofrecido como el "más probable" fue confirmado en 13 fibroadenomas, 4 cystosarcomas filoides y 3 adenolipomas. Los restantes 12 casos, entre los cuales 4 de los fibroadenomas eran microscópicos en tamaño, los cambios mamográficos descritos fueron aquellos de displasia severa sin que pudiera distinguirse la lesión dominante dentro de la densidad aumentada del seno (Fig. 3). Nos sorprendió la distribución de estos casos por edad (véase Fig. 3) ya que 24 de los 32 fibroadenomas ocurrieron entre las edades de 30 a 49 años (Fig. 4) a pesar de que tradicionalmente asociamos esta lesión con mujeres entre los 15 y los 30 años.

Figura 3

### Diagnóstico Mamográfico en Pacientes con Fibroadenoma (32)

Fibroadenoma .....	13
Cystosarcoma Phylloides .....	4
Adenolipoma .....	3
DY .....	8
QDY .....	3
Prob. maligno .....	1

Figura 4



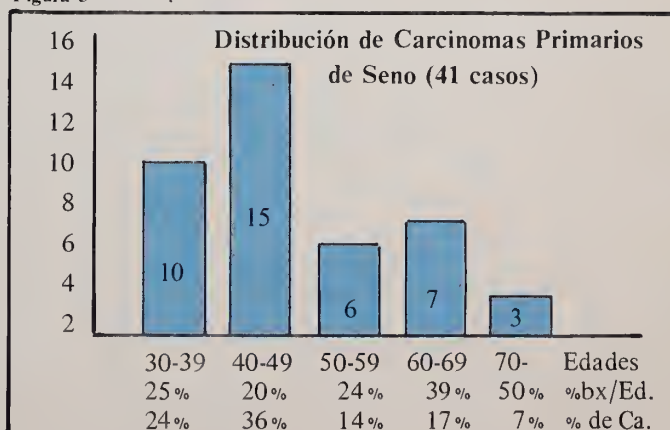
### Otros Benignos

Entre los restantes casos de lesiones benignas hubo en nuestra serie 7 papilomas intraductales 4 de los cuales eran de tamaño microscópico. De entre los 12 pacientes catalogados como "Diagnósticos Varios" en esta serie señalamos el extraño caso de granulomas por aceite mineral en una reclusa que se inyectaba este material en sus senos. La apariencia mamográfica de las colecciones de aceite era la de múltiples áreas redondas radiolucientes. Este paciente será el sujeto de una "presentación de caso" en el futuro. También en este grupo cabe señalar que la biopsia de 8 de estas pacientes fue reportada como "normal". En 3 de estas la lesión en cuestión no fue removida según fue constatado por una mamografía de seguimiento.

### Malignidades

Cuarenta y dos casos de lesiones malignas fueron encontradas en este grupo de 176 pacientes sometidas a biopsia. Fuera de un caso de rabdomiosarcoma metastático o seno en una joven de 16 años, todas las lesiones restantes (41 casos) eran lesiones primarias de seno. El 60% de los casos de carcinoma primario de seno en esta serie ocurrió entre las edades de 30 a 49 años (Fig. 5) cosa que pudiera explicarse

Figura 5



parcialmente en base a que el aumento mayor del cáncer de seno que se ha observado en P.R. y otros países es en estas edades en particular y parcialmente también por el hecho de que las mujeres sobre los 65 años y que cuentan con beneficios del seguro social (Medicare) acuden a centros hospitalarios privados con mayor frecuencia que a los centros gubernamentales (véase Fig. 1) Cuarenta de los 41 carcinomas primarios de seno eran malignidades de origen intraductal infiltrativo y solo una de las lesiones era del tipo histológico lobular (Fig. 6).

Figura 6

#### Histopatología de 41 Primarios de Seno

"Infiltrating duct cell" .....	40
Medular .....	4
Coloide .....	2
Intracístico .....	1
Inflamatorio .....	2
Paget .....	2
Lobular .....	1

Ocho de nuestras pacientes con carcinoma (19%) eran casos de carcinoma bilaterales. De estos 8 carcinomas bilaterales 4 ocurrieron en el seno remanente en pacientes con mastectomías previas entre 2 y 5 años post primera mastectomía. La mamografía fue positiva para carcinoma en estos 4 casos mientras que el examen clínico fue positivo en una y negativo en 3. La importancia del seguimiento mamográfico del seno remanente en este grupo de pacientes se enfatiza. Los restantes 4 casos con carcinomas bilaterales fueron simultáneos. En este grupo de carcinomas bilaterales simultáneos la mamografía fue positiva en 6 de las lesiones y negativa en 2 mientras que el examen clínico fue positivo en 4 y negativo en 4 de las lesiones.

#### Correlación Mamográfico-Patológica

Para propósitos de establecer nuestro grado de acierto en el diagnóstico mamográfico del grupo de pacientes con malignidad (42 pacientes) le asignamos a la interpretación original de la mamografía de estos una gradación del 1 al 5 (véase Fig. 7) indicando nuestra opinión diagnóstica y la confianza que teníamos en la misma desconociendo el diagnóstico patológico en el momento de asignar esta gradación.

Figura 7

#### Opinión Mamográfica (1 al 5)

- (1) Normal o benigno
- (2) Probablemente benigno
- (3) Indeterminado - biopsia recomendada
- (4) Probablemente maligno
- (5) Maligno

Nuestro diagnóstico mamográfico fue falso negativo en 3 casos a 2 de los cuales le habíamos asignado un número 1 y a uno un número 2. Nuestra interpretación de "indeterminado" (No. 3), la asignamos a solo un caso de estos 42 carcinomas mientras que en los restantes 38 casos o sea el 93% nuestro diagnóstico de "probablemente maligno" en 12 y "definitivamente maligno" en 26 fue confirmado (Fig. 8). El examen clínico en estos 42 carcinomas tuvo un falso negativo de 19% y un verdadero positivo de 81% (Fig. 9) demostrándose así el inmenso valor de la mamografía como método sensitivo y específico para el diagnóstico de cáncer de seno. Cabe señalar que el por ciento de falsos negativos en las mamografías y en el examen clínico de estos pacientes es ciertamente aceptable en comparación a las numerosas series informadas por otros autores en todo el mundo.

Figura 8

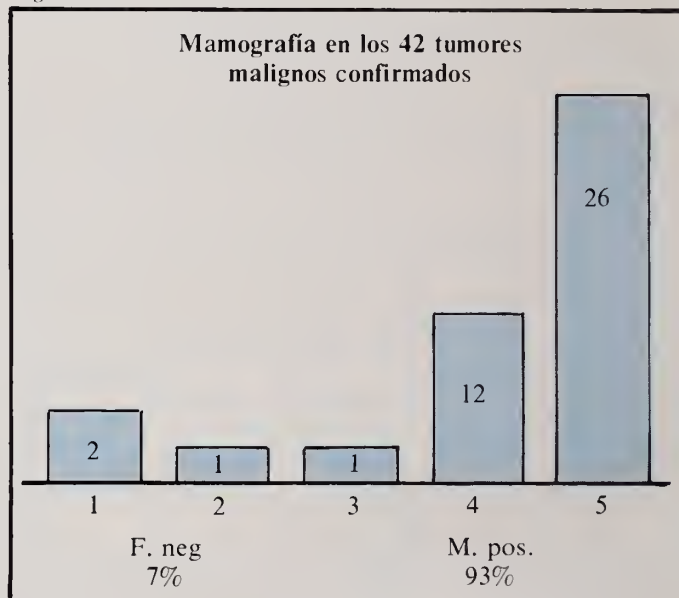
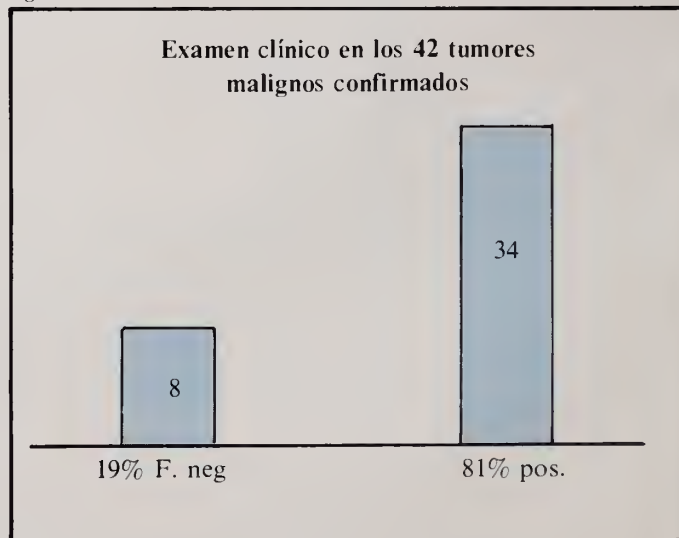


Figura 9



En 2 de los casos considerados falsos negativos por mamografía, la lesión no se incluyó en el estudio por su localización posterior y adherencia a la pared costal. Para minimizar la posibilidad de otros falsos negativos debido a esta razón, comenzamos en enero de 1982 a utilizar la vista oblicua modificada en substitución de la vista medio-lateral,



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con lo cual se obtiene una visualización más completa de la región retromamaria en la inmensa mayoría de los pacientes. El otro falso negativo ocurrió en un paciente con cambios severos de displasia y múltiples quistes dominantes donde la lesión no fue descubierta ni clínica ni mamográficamente apareciendo en la pieza patológica en medio de un grupo de quistes dominantes.

Utilizando el sistema de gradación ya descrito (véase Fig. 7) encontramos 27 casos de falsos positivos por mamografía en la serie de los 176 pacientes sometidas a biopsia. Un repaso de la mamografía y la patología en estos casos nos hizo ver que en 16 de ellos la patología benigna descrita explicaba adecuadamente los hallazgos sospechosos de malignidad (Fig. 10). Sin embargo en los 11 casos restantes, la patología no explicaba los hallazgos sospechosos de malignidad vistos en la mamografía. Estos 11 casos así identificados serán re-evaluados como ya lo han sido otros 8 casos en las mismas circunstancias 6 de los cuales fueron sometidos a una segunda biopsia resultando 4 de ellos tener en efecto un carcinoma. La utilización de este sistema para identificar y propiciar la re-evaluación de los casos en que la patología no concuerda o explica los hallazgos mamográficos sospechosos de malignidad, es en nuestra estimación una de las mayores aportaciones de la División de Mamografía al mejor manejo de estos pacientes.

Figura 10

#### 16 "Falsos Positivos" con explicación patológica aceptable

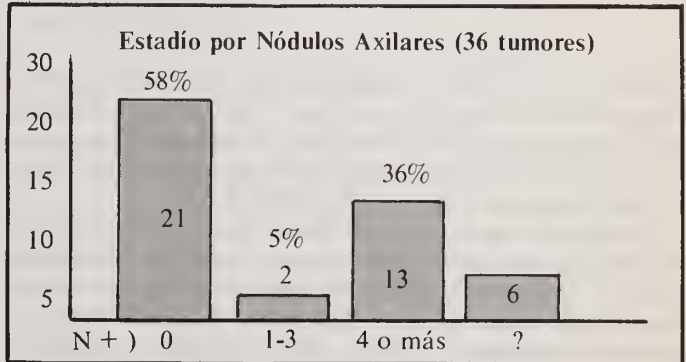
EFQ.....	6
Adenosis esclerosante o mazoplasia .....	6
Abceso y-o mastitis .....	3
Ectasia ductal .....	1

#### Estadio

El estadio de las lesiones por nódulos axilares fue evaluado en los 36 casos en los cuales 15 o más nódulos fueron removidos al momento de la mastectomía. Las restantes 6 pacientes no fueron evaluados en cuanto a estadio por haber información insuficiente en relación a los nódulos axilares en su expediente o por haberse removido menos de 15 nódulos al momento de la cirugía. En 21 pacientes (58%) los nódulos axilares eran negativos para malignidad. Dos pacientes (5%) tenían de 1 a 3 nódulos axilares positivos. Trece pacientes (36%) tenían 4 o más nódulos axilares envueltos (Fig. 11). Es decir, el 63% de los pacientes evaluados en cuanto a estadio en esta serie fueron descubiertos en un estadio temprano. El descubrimiento de este alto por ciento de mujeres en estadio temprano representa un adelanto extraordinario en este renglón particularmente si lo comparamos con la serie de carcinomas de mama investigadas en la pasada década en este mismo centro donde la inmensa mayoría de los pacientes eran descubiertos en estadios avanzados de su enfermedad.<sup>7</sup> El alto por ciento de estadios tempranos en este grupo de pacientes obedece a nuestro entender a varias razones entre las cuales está el mayor conocimiento y toma de conciencia por parte de los pacientes en relación al cancer de mama, el "expertise" de los cirujanos envueltos y su confianza en nuestros hallazgos mamográficos, el personal de enfermería de extraordinaria dedicación en esta clínica, y ciertamente la mamografía de alta

calidad. Entendemos que la experiencia aquí redactada podría servir como base a un protocolo de evaluación y seguimiento de mujeres con signos y síntomas de enfermedad de los senos y como un estímulo a aumentar y mejorar el uso de la mamografía dentro y fuera de las facilidades gubernamentales.

Figura 11



**Resumen:** Hemos presentado nuestra experiencia con 1200 casos de la Clínica de Enfermedades del Seno del Hospital Universitario referidos a nuestra División para mamografía. Esperamos que la misma sirva de base para comparar otras experiencias en Puerto Rico así como la futura experiencia nuestra. Entendemos que este es el primer grupo con correlación mamográfica patológica reportado en el país. En nuestro análisis hemos confirmado el valor de la mamografía y la División dedicada a ella en el Centro Médico de P.R. En nuestras manos la mamografía ha probado ser un método de diagnóstico de extraordinaria sensibilidad y especificidad. Nuestra División y este estudio han servido además, como un taller de entrenamiento para residentes de Radiología y tecnólogos radiológicos en la modalidad de mamografía. Finalmente entendemos que hemos desarrollado un modo efectivo de identificación para re-evaluación de aquellas pacientes en las que hay un alto grado de sospecha de malignidad por mamografía, y en las cuales la patología con la biopsia inicial no correlaciona con el hallazgo mamográfico. El alto grado de positividad en un grupo de pacientes que ha sido así identificado y re-evaluado, justifica este esfuerzo.

#### Recomiendamiento

Agradecemos profundamente a las Sras. Myrta Cotto, R.N. y Noemí Cruz, R.N. de la Clínica de Enfermedades del Seno del Hospital Universitario y a la Sra. Elba Marrero, R.T. de la División de Mamografía del CMPR, la excelencia profesional, la dedicación y el humanismo con el que realizan sus labores. Estas hicieron posible no sólo el presente estudio sino también permitieron proporcionar el mejor cuidado posible a estos pacientes.

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6. Sra. Myrta Cotto, R.N.; Sra. Noemí Cruz, R.N.
7. Comunicación personal Dra. Olga Rodríguez y Dr. Reynold López.



# Malignant Melanoma in Puerto Rico

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Sheila M. Torres, MS IV  
Jorge L. Sánchez, M.D.

**Summary:** A study of malignant melanoma among native Puerto Ricans informed to the Puerto Rico Cancer Registry between the years to 1980 is reported. A total of 127 new cases were documented and the annual incidence ranged from 7.5 to 11.3 per million inhabitants with a mean of 9.22.

Tumors were more frequently located in volar and subungual skin sharing these predilection with other races like Blacks and Japanese. The clinicohistologic type most frequently recognized was the superficial spreading melanoma (16.2%) followed by nodular melanomas (14.7%), acral lentiginous melanoma (10.%) and lentigo maligna melanoma (3%). Metastatic melanomas constituted 3.1% of the total of cases.

One important aspect of the study is that fifty one percent of the cases were reported pathologically under the broad term of malignant melanoma with no reference to the clinicohistologic type. Clark's levels of invasion were included in 48% of the cases and Breslow's thickness of the tumor in only 6%. In order to have a better assesment of survival from malignant melanoma in our population, an effort should be made by those involved in the management of these patients to better correlate findings in melanoma tumors according to the different parameters.

In 1967, Pantoja et al<sup>1</sup> reported a total of 119 cases of malignant melanoma among native Puerto Ricans managed at one of the main cancer centers in the island between 1948 and 1972. Fifty seven were located on the lower extremities of which forty nine cases (41.1%) were on

the feet with the soles being the most common location.

Since it is our clinical experience that by anatomic location, malignant melanomas in Puerto Ricans are more frequent in volar and subungual skin, and that the clinicohistologic type of these melanomas is invariably acral lentiginous melanoma,<sup>2</sup> we decided to collect all the available data of all melanoma cases in Puerto Ricans diagnosed between 1977 and 1980 from the Puerto Rico Cancer Registry for a better assesment of such estimates.

## Material and Methods

All malignant melanoma cases reported to the Puerto Rico Cancer Registry between 1977 and 1980 are included. Cases from 1981 are not included because complete data was not available at the time of this study. Recorded data included age, sex, anatomic location, clinical description, and pathologic report. They were divided among the current classification of clinicohistologic types of malignant melanoma<sup>3</sup> looking with special emphasis for Clark's level of invasion and Breslow's thickness of the tumor. A tumor was listed as unclassified if the pathologic report only categorized the tumor as a malignant melanoma without mentioning clinicohistologic type. Tumors were listed as metastatic if no evidence of the primary lesion was found but metastasis were their presenting manifestations. One case was listed as "unknown" because the histologic features were not definitely diagnostic of melanoma and an undifferentiated carcinoma was a possibility. Cases of lentigo maligna were excluded from the series since they are considered as a precursor or the in situ phase of lentigo maligna melanoma. Three patients from the Virgin Islands were also excluded from this report.

## Results

A total of 127 new cases of malignant melanoma were reported in Puerto Rico during this period representing a rate of 9.22 per million population per year. There were 25

TABLE I\*

Anatomic Site	1977	1978	1979	1980	Total
Head & Neck	6	4	7	7	24
Chest	0	1	2	5	8
Back	4	1	4	5	14
Arms	4	4	2	6	16
Abdomen	1	2	0	2	5
Buttocks	0	2	0	0	2
Thighs	1	1	2	6	10
Legs	2	1	5	0	8
Hands	0	1	3	0	4
Feet	7	7	11	10	35
Unknown	0	2	0	1	3

\* Two patients had two different primary tumors.

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cases in 1977, 26 in 1978, 36 in 1979 and 40 in 1980 with a mean of 31.7 of new cases per year. The annual incidence per million inhabitants was 7.5 in 1977, 7.7 in 1978, 10.4 in 1979, and 11.3 in 1980. There were 64 males and 63 females for a ratio of males to females of nearly 1 to 1. The ages ranged from 23 to 108 years.

Table I lists the total numbers of cases according to anatomic location. The feet was the most frequent location



of melanomas with 35 cases (27%), followed in decreasing order of frequency by the head and neck with 24 (18.0%), the arms 16 (12.4%), the back 14 (10.8%), thighs 10 (7%), the legs and chest with 8 each (6%), abdomen 5 (3%), hands 4 (3%) and buttocks with 2 (1.5%). In three cases the affected area was not specified. Acral areas as a group (feet 35, hands 4) comprised a total of 39 cases representing 30.2% of the total.

Table II lists the number of cases according to clinicohistologic type. Sixty-six of the cases were unclassified representing 51.1%. Superficial spreading melanoma was the most frequent clinicohistologic type recognized with 21 cases (16.2%) followed by nodular melanoma type with 19 (14.7%), acral lentiginous melanoma 13 (10%), lentigo maligna melanoma with 4 (3%), and in one case it could not be established. Metastatic melanomas to skin or lymph nodes in which the primary lesion was not identified after complete evaluation constituted a total of 5 cases (3.1%).

Clark's levels of invasion were included in the pathologic report in 62 out of 129 lesions (48%) and Breslow's thickness of the tumor was only reported in 9 of the cases (6%).

to the different parameters. The pathologic report of malignant melanoma should therefore include clinicohistologic type, level of invasion, tumor thickness, cellularity of the tumor, host cell response and presence or absence of ulceration.

Acral lentiginous melanoma described by Reed in 1975, is a clinicohistologic form of cutaneous malignant melanoma characterized grossly by a lentiginous appearance and histologically by atypical spindle-shaped and epithelioid melanocytes in the epidermis and dermis.<sup>3 6 8</sup> Acral lentiginous melanoma may be confused histologically with lentigo maligna melanoma, but its biologic behavior is analogous to superficial spreading melanoma as noted by Clark et al.<sup>6</sup>

It is interesting to note that this clinicohistologic type, although recently recognized, constituted 22.8% of the total of cases in which a specific clinicohistologic type was reported. This should be no surprise as this type is only reported to occur in volar areas and nailbeds which in our study constituted the highest percentage of cases. It is known that the incidence of acral lentiginous melanomas varies according to race.<sup>9</sup> Blacks and Japanese are among the most frequently

TABLE II\*

Classification	1977	1978	1979	1980	Total
Superficial spreading	3	4	7	7	21
Nodular	5	5	3	6	19
Lentigo Maligna Melanoma	0	0	2	2	4
Acral Lentiginous	2	2	4	5	13
Unclassified	14	15	20	17	66
Metastatic	1	0	0	4	5
Unknown	0	0	0	1	1

\* Two patients had two different primary tumors.

## Discussion

Malignant melanoma are generally divided by clinicohistologic features into five types, namely, superficial spreading melanoma, lentigo maligna melanoma, nodular melanoma, acral lentiginous melanoma and mucosal melanoma.<sup>3</sup> Polypoidal, verrucous, and other miscellaneous malignant melanomas constitute other less common clinicohistologic presentation.<sup>3 5</sup>

One of the main aspects in the findings of this study is the extremely high number of tumors labeled in the broad term as "malignant melanoma" and listed as unclassified in this study because no clinicohistologic type was specified. Also in more than half of the cases Clark's levels of invasion were not reported and even more is the fact that in only 6% of the cases Breslow's tumor thickness was reported. It is known that the prognosis of malignant melanoma depends on a series of factors including tumor thickness, levels of invasion, anatomic site, ulceration and the clinicohistologic type.<sup>6</sup> In order to have a better assessment of survival from malignant melanoma in our population, an effort should be made by those involved in the management of these patients to better correlate findings in melanoma tumors according

affected while in Caucasians the incidence is much lower.<sup>9 10</sup> A prospective and retrospective clinicopathologic study of melanomas in acral locations in Puerto Ricans has recently shown that the histology of such tumors is invariably that of acral lentiginous melanoma.<sup>2</sup> Thus, it seems that Puerto Ricans share with Blacks and Japanese the tendency to present such type of melanomas. As this type of melanoma is more widely recognized in the island, many more cases will be diagnosed annually and will probably be the most common clinicohistologic type recognized.

Melanoma in blacks usually spare pigmented skin and most commonly involve the lighter palms and soles.<sup>9</sup> The role of trauma associated with walking barefoot has been emphasized as a possible etiologic factor in these cases. Urbanization and the protection afforded by shoes, however, have not decreased the incidence of melanoma in African tribes.<sup>11</sup> Barefootedness is unusual among both native Puerto Ricans and American Negroes, so the reason for this propensity remains speculative and other factors must account for the observed site predilection.

The roles of trauma in the transformation of a nevus to a melanoma also remains unsettled.<sup>12</sup> There is no definite data indicating the frequency and types of melanocytic lesions in

acral areas which become malignant.<sup>13</sup> Since there are numerous dermatologic conditions that can mimic melanoma clinically and since the diagnostic accuracy of melanoma ranges in five different series between 23.5% to 64.4%, we recommend removal, with conservative margins, of any irregularly shaped or colored, congenital or acquired, pigmented melanocytic nevus in acral areas of adults.<sup>14</sup> The preceding is particularly significant since the most frequent location of melanoma in Puerto Ricans is in volar and subungual skin.

**Resumen:** Se presenta un estudio de los casos de melanoma maligno en puertorriqueños reportados al Registro de Cáncer de Puerto Rico en los años 1977 a 1980. Se documentan un total de 127 casos durante este período, la incidencia anual fluctuó entre 7.5 a 11.3 por millón de habitantes con un promedio de 9.22.

La localización anatómica más frecuente fue en el área volar y en el lecho ungueal compartiendo esta tendencia con otras razas como los Negros y los Japoneses. El tipo clinicohistológico más frecuente encontrado fue el de melanoma superficial expansivo (16.2%) seguido del melanoma nodular (14.7%), melanoma acral lentiginoso (10%) y el de melanoma maligno lentiginoso (3%). Melanomas metastásicos constituyeron el 3.1% del total de casos.

Un aspecto importante de este estudio es que el 51% de los casos fueron reportados como melanoma maligno sin referencia alguna al tipo clinicohistológico. Los niveles de invasión de Clark se reportaron en un 48% del total de casos y el grosor de tumor de Breslow en solo 6%. Para poder tener un mejor estimado de la sobrevida de melanoma maligno en nuestra población, se debe de hacer un esfuerzo por todos los que manejan pacientes con la condición en correlacionar los hallazgos en melanoma de acuerdo a los parámetros establecidos.

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## SIRVIENDO AL PUEBLO Y A LA PROFESION MEDICA



ASOCIACION MEDICA DE PUERTO RICO



# Congenital Hypertrophic Pyloric Stenosis: Experience at the Ponce Regional Hospital

José Ortiz Rosado, M.D.  
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**Summary:** A retrospective record review study was carried out for cases of pyloric stenosis managed at the Ponce Regional Hospital between 1970-1980. The clinical presentation, physical findings, and diagnostic methods were similar to those well established for this condition. The data on the surgical treatment (Ramsted pyloromyotomy) confirm the excellent results reported worldwide for this approach with minimal complications and no mortality.

Congenital hypertrophic pyloric stenosis is one of the commonest surgically treated conditions of the first few months of life. The incidence has been reported as between one in three hundred to one in nine hundred live births.<sup>1,2</sup> Effective surgical treatment dates to the beginning of the century when Fredet suggested that the pyloric muscle be split without division of the mucosa (1907); and this was followed by Ramsted's performance and description of a similar operative procedure (1912).<sup>3</sup> Several institutions have reported their experience with pyloric stenosis and its surgical treatment.<sup>1,2,3</sup> We became interested in reviewing the local experience with this condition at our institution.

## Materials and Methods

A retrospective record review study was carried out for all cases of pyloric stenosis at the Ponce Regional Hospital. Between 1970 and 1980 a total of 131 patients with this diagnosis were operated. Of these, 96 patients records were retrieved and reviewed; the remaining records were unobtainable. The reviewed records were analyzed for data on the onset and type of symptoms, physical findings, diagnostic methods, operative procedure, complication, length of hospitalization, and mortality or other outcome. Clinical laboratory tests including the complete blood count and serum electrolyte levels were analyzed. These data forms the basis for this report.

## Results

There were 131 records with a recorded diagnosis of pyloric stenosis. Of these, 96 records were obtained and reviewed. The remaining records were lost and not available for analysis. There were 82 male (85.4%) and 14 females

(14.6%). the onset of symptoms occurred at a median age of 30 days (33.5 days average). The order of birth of the affected child was as follows: first-born 23 (33.9%), second-born 27 (28.1%), third-born 16 (16.6%), fourth-born (13.5%) and fifth and subsequently-born 17 (17.7%). The clinical picture included symptoms of vomiting in 96 (100%), diarrhea in one (1%) and fever in two (2%). On physical examination there were signs of dehydration in 18 (19%); reverse peristaltic waves were noted in seventy four (77%); a "pyloric olive" was palpable in 86 (90%); abdominal distension was present in six (6%) and jaundice was noted in one (1%). In 32 cases a barium upper gastro intestinal series was performed, and the study was diagnostic for pyloric stenosis in all instances (100%). There were no instances of either false positive or false negative studies recorded in this group of children.

Complete blood counts obtained revealed that in 14 cases the hematocrit was below 32%, and in 33 cases it was above 40%, no data was recorded in 15 cases. White blood counts were above 10,000 in 62 cases; within the range of 5 to 10,000 in 31, and not recorded in 3 cases. Serum electrolytes were obtain in some patients. Serum sodium was below 136 meq/liter in 27 patients and were within the normal range of 137 - 145 meq/liter in 13 other patients. There was no sodium level recorded in 56 cases. Chloride was less than 96 meq/liter in 12 cases; from 96-110 meq/liter in 14 cases; not recorded in 70 cases. Potassium level was below 3.3 meq/liter in 4 cases; in the normal 3.4-5.0 meq/liter range in 27 cases and above 5.1 meq/liter in 10 cases. Bicarbonate levels were recorded in the normal range of 24 - 32 meq/liter in 6 cases, below 23 in 5 and above 33 in 3.

All patients reviewed underwent a standard Ramsted-type pyloromyotomy. No other procedures were performed in these patients. Postoperatively, oral feedings were started within 12 hours in 7 cases; from 12 to 24 hours in 33 cases; from 24 to 48 hours in 30 cases; and after 48 hours in 26 cases. Postoperative complications were mostly infectious: wound infection (3), clinical sepsis (1), bacteremia (1), pneumonia (1) and fevers which resolved spontaneously (3). There was transient postoperative vomiting in 4 patients but this resolved spontaneously in all. One case developed a prolonged paralytic ileus, and another a wound evisceration. There were no cases of postoperative bleeding or of intraoperative mucosal perforation. There were no deaths.

The median time from hospitalization to diagnosis was one day (2.79 days average). Similarly the median length of time from diagnosis to operation was one day (average 1.67 days), and the median length of time from operation to discharge was 6 days (average 7.22 days).

## Discussion

The clinical picture that emerges from our review of 96 cases of pyloric stenosis is similar to that reported from other institutions.<sup>1,2,3,4</sup> The marked male predominance was confirmed (85% male) although the reported higher incidence in first-born children was not born out in our experience. The onset of symptoms occurred within the usually described period of 2 to 6 weeks of age. The clinical presentation with non-bilious vomiting as the predominant sign was similar. The physical signs of a palpable "pyloric olive" (90%), reverse peristalsis (74%) and dehydration (19%) were commonly described.

Diagnostic workup included a barium upper gastrointes-

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tinal series in 32 cases. These studies were diagnostic in all cases, without false positive or false negative results. This confirms the previously reported high degree of accuracy of this radiologic study. Other diagnostic methods such as sonography were not utilized.

The reported chemical abnormalities due to persistent vomiting were documented in a significant number of our patient. Hyponatremia, hypochloremia and hypokalemia were common in those cases where electrolyte levels were obtained preoperatively.

The definitive diagnosis was made within a short period of time from hospitalization (median within one day). Similarly the time from diagnosis to operation was short (median one day). During this period maneuvers to correct dehydration and/or electrolyte abnormalities were carried out prior to operation. The median length from operation to discharge (6 days) appears somewhat prolonged as compared to other reports.<sup>1-4</sup>

The results of the Ramsted-type pyloromyotomy, which was performed in all cases, confirm the efficacy and relative safety of this procedure. There were no reported deaths. There were no reports of major complications such as post operative bleeding or intraoperative mucosal perforation. The main complications were infectious, probably preventable in most instances. Post operative vomiting occurred in a small percentage of patients, well within the reported incidence for these minor vomiting problem.<sup>5</sup>

Feeding was started as early as within 12 hours in some and within 24 hours in approximately 40% of cases, without problems. This reinforces the practice of early refeeding of these infants in the postoperative period. However, a significant group (25%) was held without feeding for over 48 hours, in most cases without apparent reason. Pulmonary

complications were reported in one case, probably related to aspiration during the procedure.

In general, these data confirm the excellent results for this operation reported worldwide and can be contrasted to both the mortality of non-surgically treated infants (documented to be as high as 80%) and to that following other types of surgical procedures, such as gastrojejunostomy (approximately 50%).<sup>5</sup>

**Resumen:** Se llevó a cabo un estudio retrospectivo de revisión de expedientes para casos con estenosis pilórica tratados en el Hospital Regional de Ponce durante el período de 1970-1980. La presentación clínica, los hallazgos físicos, y los métodos diagnósticos utilizados fueron similares a los anteriormente establecidos para esta condición. Los datos concernientes al tratamiento quirúrgico (piloromiotomía de Ramsted) confirman los resultados excelentes que se reportan mundialmente con dicho abordaje, al encontrarse un mínimo de complicaciones y ninguna mortalidad.

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## CALCIUM BLOCKER INDICATIONS CITED

It is appropriate and legal for physicians to prescribe approved drugs for uses not included in their official labeling when such uses can be supported as rational and accepted medical practice, said a report on calcium channel blocking agents.

The report, prepared by the AMA's Council on Scientific Affairs and approved by House of Delegates, discusses the indications for use of the calcium blocking drugs, which can dilate the coronary blood vessels that carry oxygen and nutrients to the heart muscle and can slow the heartbeat rate.

Pointing out that some of these drugs are selectively more effective in one type of tissue than another, the report notes that some experimental results suggest that certain agents may prove effective in limiting the extent of damage to the heart muscle during a heart attack.

Concluding that there is a "wide spectrum of cardiovascular and other disorders that may also respond" to these agents, the reports says, "It will probably take years before the final role of each of these drugs, in the various indications that have been proposed, will be established".

"Many patients have a growing sense of impersonalization and fragmentation. They go to their doctors' offices seeking refuge from their fears and loneliness and do not adjust easily to new encounters, either with those who preside over separate domains in medical science or with highly sophisticated marvels of diagnostic technology. The conclusion is clear: doctors who spend more time with their patients may have to spend less money on malpractice insurance policies.

Norman Cousins, Author, at graduation ceremonies, Tulane University, Medical Society County of Erie, July 1982.

Tokyo, with effective gun control, has about 500 homicides and armed burglary cases a year, while New York City (with nearly 4 million fewer population) has 85,000 cases - about 150 times as many.

Sidney Harris.



# Kidney Transplantation Does Not Halt The Progression of Secondary Complications of Insulin Dependent Diabetics An Open Question

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**Abstract:** This study evaluated the objective and subjective changes in the secondary complication of diabetes mellitus experienced by insulin dependent diabetic patients receiving renal transplants at our center. Twenty-five kidney allografts performed in 23 patients were included in our retrospective review of the cases.

The results of this analysis indicated that kidney transplantation alone did not appear to halt the progression of the secondary complications of diabetes mellitus in the majority of these patients. Perhaps combined kidney and pancreas transplantation might provide better control of the progression of these secondary complications.

Renal transplantation has been recommended as the treatment of choice, for end stage renal disease due to type I diabetes.<sup>1</sup> It was previously suggested that insulin dependent diabetics did poorly in hemodialysis with respect to the progression of their associated secondary complications, such as retinopathy and neuropathy.<sup>1</sup> In contrast, some renal transplant centers reported, at least, a stabilization of various secondary complications in diabetics after cadaveric kidney transplantation.<sup>2</sup> Our study was directed at evaluating the objective and subjective changes in the secondary complications experienced by insulin dependent diabetic patients receiving cadaveric renal transplants at a single center.

## Materials and Methods

Twenty-five kidney transplants performed in 23 patients with diabetic nephropathy between October, 1979 and December, 1981 at Mount Carmel Mercy Hospital, were included in this study. Twenty-two patients received primary cadaveric renal transplants and three received second cadaveric transplants. The demographic data for the entire group of patients are shown in Table I. Our patients represented a high risk patient population for transplantation, similar to the one described in previous publications.<sup>3,4</sup> The type and characteristics of our immunosuppressive regimen which

consisted of azathioprine, low doses of steroids and anti-lymphoblast globulin (ALG) has also been previously published.<sup>3,4</sup> A non-deliberate blood transfusion protocol was used, and there were no splenectomies performed. Patient medical histories were carefully reviewed to determine not only the status of diabetic secondary complications, but to assess also, 1) patient survival, 2) graft survival, 3) rates of infectious complications and 4) change of insulin requirements following renal transplantation.

TABLE I

Demographic Data on 23 Insulin Dependent Diabetic Recipients of Cadaver Kidney Transplants	
<u>Duration of Diabetes</u>	<u># of Patients</u>
10 - 20 years	14
> 20 - 26 years	9
<u>Age at Transplant</u>	
< 30 years	7
30 - 40 years	5
> 40 years	11
Range: 21 - 58 years	
Mean: 41.2 years	
<u>Sex</u>	
Males	16
Females	7
<u>Race</u>	
Black	15
White	8

## Objective Evaluation of Secondary Complications of Diabetes

The pre-transplant work-up on uremic diabetics included in most of the patients, a complete assessment of all target organs. The upper gastrointestinal tract was primarily evaluated by an upper gastrointestinal series, and small bowel follow through x-rays were occasionally performed. Nerve conduction studies were carried out on the median, peroneal and posterior tibial nerves to measure conduction velocity and distal latency. Vascular studies included doppler peripheral studies and angiograms when indicated. Myocardial imaging (MUGA scan) was performed to assess left-ventricular function and heart performance. Ophthalmological consultation included fluorescein angiography, assessment of corrected visual acuity, and overall assessment of the eye fundii. Cystoscopic studies with voiding cystometrourethrograms (VCMUG) were carried out to evaluate the bladder and urinary tract. Periodic follow-up studies of these tests were performed at various intervals in different patients, preferably at 6 and 12 months after transplantation, and on few occasions at 18 months post-transplant.

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Changes in the evaluation of the secondary complications were divided into three categories as improved, deteriorated or unchanged.

### Subjective Evaluation of Secondary Complications of Diabetes

An extensive subjective survey was conducted by two physicians to evaluate the differences in the secondary complications of diabetes mellitus present in these patients before and after transplantation. The surviving patients, or the families of the deceased patients were contacted and asked questions related to common diabetic symptomatology pertaining to the development of secondary complications. Each respondent evaluated the changes in the following areas 1) peripheral neuropathy, 2) retinopathy, 3) vascular disease and, 4) visceropathy. Answer were tabulated in three categories as improved, deterioration or unchanged, compared to the condition of the secondary complication prior to transplantation.

Special attention was directed at maintaining a tight control of peripheral blood sugar by a rather frequent self blood glucose monitoring and adequate insulin coverage. Also, the blood pressure was self-measured several times a day in order to improve the control of blood pressure, with a satisfactory medical management.

### Results

Figure 1 shows the actuarial patient and graft survival following cadaver kidney transplantation. Three of 23 patients survived less than 6 months post-transplantation. Table II shows the causes of death for all patients who expired during the whole follow-up period. Three patients died with functioning grafts.

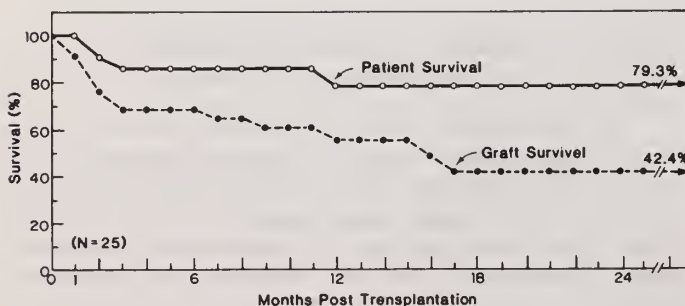


Fig. 1: Actuarial graft and patient survival one year after cadaver kidney transplantation on patients with insulin dependent diabetes.

Five patients did not show any change in the requirements of insulin, seventeen patients (73%) observed an increase in the need of insulin ranging from 5 to 78U from the previous values, and one patient showed a decrease of 8U in the requirements of insulin.

TABLE II

### Cause of Death of All Type I Diabetics Receiving Kidney Transplants

Cause of Death	# of Patients
Pneumonia, functioning graft	1
Pneumonia, uremia	1
Pulmonary emboli, functioning graft	1
Cumulative effects of uremia & rejection	1
Cumulative effects of diabetes	1
Unknown, functioning graft	1
	6

Table III shows the infectious complications seen after transplantation. Seven out of twenty-three patients (30%) developed infectious complications at one point during the follow-up period.

TABLE III

### Frequency of Infection Complications After Transplantation

Infection Complications	# of Cases
Pneumonia	2
Monilial esophagitis	1
Urinary tract infection	1
Perianal abscess	1
Leg abscess (Staph)	1
Post-operative wound infection	1

Figures 2 and 3 show the status of the secondary complications from the objective and subjective points of view at one year post-transplantation. It is obvious that in most of the categories, there was no improvement seen in the outcome of the secondary complications. Also, from the objective point of view, less improvement was noted when compared with the subjective observations. A subjective deterioration

### Status of Secondary Complications of Insulin Dependent Diabetics at One Year After Kidney Transplantation

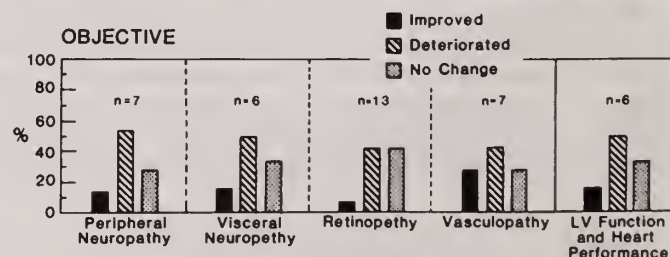


Fig. 2: There was no objective improvement on the secondary complications of insulin dependent diabetics after cadaver kidney transplantation. If anything, a higher incidence of deterioration was observed.



of retinopathy was also seen, as well as some improvement on the visceral neuropathy. There is no clear explanation for this last finding. From the vascular point of view, two patients out of 23 (8%) required distal amputation within one year of follow-up. Another patient required a femoro-popliteal saphenous vein bypass for severe arteriosclerotic peripheral vascular disease.

**Status of Secondary Complications  
of Insulin Dependent Diabetics at  
One Year After Kidney Transplantation**

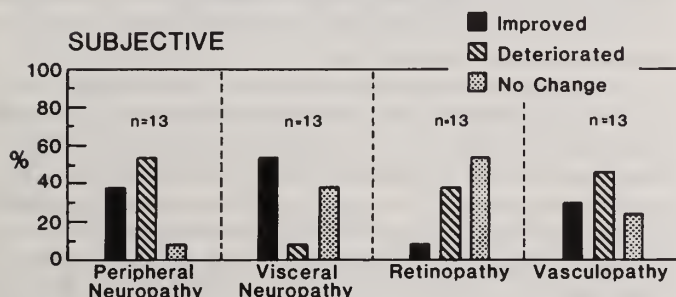


Fig. 3: In general, the subjective evaluation of the secondary complications of insulin dependent diabetics after kidney transplantation followed the same pattern observed from the objective point of view. That is, more deterioration and lack of improvement was noted, except for the visceral neuropathy changes.

### Discussion

The results of this study shows that the diabetic patients at our center experienced variable objective and subjective changes in the secondary complications of their diabetes after receiving cadaveric renal transplants. It is clear, however, that kidney transplantation alone did not appear to halt the progression of the secondary complications of diabetes mellitus in the majority of these patients. The effect of kidney transplantation was evident in the reversal of uremia, but not in the general improvement of the diabetic condition. Our preliminary results do not appear to be in accordance with other centers<sup>1-6</sup> that have reported improvement or significant stabilization of one or various secondary complications.

The frequency of infectious complications in this group was higher than the one observed in the non-diabetic group at our center. However, our patient population did not have the variety of septic problems reported at other centers.<sup>2</sup>

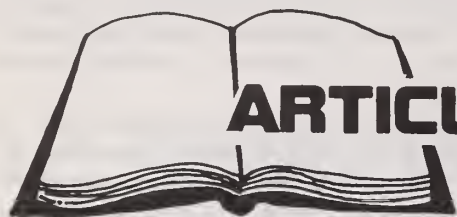
In summary, renal transplantation is a good alternative therapy for the management of the diabetic end stage renal disease. However, improved kidney function alone does not consistently halt the progression of many of the secondary complications of diabetes in these patients. Even though the alternative to renal transplantation is currently improved dialysis methods, it is possible that the combination of kidney and pancreas transplantation could offer some help to the diabetic patient, when some of the difficulties currently existent with pancreatic transplantation can be solved. Also, it is feasible that better glycemic control by more tight insulin administration or even early pancreatic transplantation might be the long time waited therapy for the insulin dependent diabetic.

**Resumen:** Este estudio evalúa los cambios objetivos y subjetivos en la complicación secundaria de diabetes mellitus en aquellos pacientes, insulino-dependientes sometidos a trasplante renal. La serie incluye 23 pacientes sometidos a trasplante en nuestro centro.

Los resultados indican que el trasplante renal de por sí no detiene la progresión de las complicaciones secundarias de diabetes mellitus en la mayoría de ellos. Postulamos que quizás los trasplantes combinados de riñón y páncreas puedan proveer un mejor control en la progresión de estas complicaciones secundarias.

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# ARTICULOS DE REPASO

## VIRAL HEPATITIS

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Currently, viral hepatitis continues to be a major public health problem and ranks fourth among the 30 nationally reported communicable diseases in the United State. This data is hampered by the fact that the accuracy of reporting in all ages is probably no better than one in every five cases.

Following Dr. Blumberg's discovery in 1965 of the Australian antigen particles in the blood of an aborigine viral hepatitis research received a major boost.<sup>1</sup> A massive amount of literature involving numerous disciplines and worldwide contributors, has accumulated.

Although many viruses are capable of producing hepatitis (coxsackie, rubella, EB, adenovirus, herpes simplex, cytomegalovirus, etc.) this article will concern itself with hepatitis A, hepatitis B, and hepatitis non-A, non-B. (Table I)

TABLE I

NEW NOMENCLATURE FOR HEPATITIS A AND B		
	Hepatitis B	Hepatitis A
Virus	HBV	HAV
Surface antigen	HBsAg	HAsAg
Core antigen	HBcAg	HAcAg
Surface antibody	Anti-HBs	Anti-HAs
Core antibody	Anti-HBc	Anti-HAc
Other core	e antigen or eAg	
particles	DNA polymerase	?
Surface antigen	a <sub>1</sub> yw, a <sub>2</sub> 1yw,	
variants	a <sub>2</sub> 3yw, ayr,	?
	a <sub>2</sub> 1dw, adyr	

### Epidemiology

Although hepatitis A can be transmitted by parenteral inoculation, the usual mode of transmission is the fecal-oral route. Epidemics frequently result from contamination by an infected individual of a food source common to a family or institution. It is important to realize that in these circumstances the history of contact with an infected individual may be difficult to establish since the ratio of subclinical, anicteric cases to icteric cases is as high as 10 to 1 in children.<sup>2</sup> Raw or inadequately cooked bivalves (oysters, clams, mussels) are another common infective source. Bivalves continually filter sea water through their intestinal canal, thereby trapping and concentrating the microparticles of their environment. Hepa-

titis A virus may thus be present in high titers in bivalves obtained from sewage contaminated beds, and bivalve ingestion has been shown to be the source of both epidemic and sporadic hepatitis A infection.<sup>3, 4</sup>

It has been estimated that for every clinically apparent case of hepatitis B occurring after blood transfusion, there are 20 subclinical (anicteric) cases.<sup>5</sup> Since type B disease is most often transmitted parenterally by inoculation of infective blood, it can therefore be appreciated that most cases will only appear sporadically. On the other hand, exposure to patients with high titers of HBsAg increase the risk of disease transmission and results in a much higher incidence of serious type B hepatitis. This probably reflects the consequences of exposure to high doses of virus.

In addition to whole blood, hepatitis B may be transmitted by blood products including fibrinogen, antihemophilic-globulin and vaccines, saliva, duodenal secretions, urine, semen, breast milk and stool. (Table II)

Hepatitis non-A, non-B have been shown to be transmitted only by the parenteral route.

TABLE II

VIRAL TRANSMISSION			
Mode	Hepatitis A	Hepatitis B	Hepatitis Non-A, Non-B
Food	+	0	0
Shellfish	+	0	0
Water	+	0	0
Primates	+	++	0
Family	++	++	0
Institutions	++	++	+
Parenteral	+	++	++
Transfusion	0	+	++
Hemodialysis	0	++	+
Oral	++	±	0
Venereal	0	+	0
Vertical			
(mother-newborn)	0	+	0
Transplantation	0	+	++

0=never reported; +=infrequent; ++=common; ±=unclear.

### Pathogenesis

While it had been considered that all animals, except man, are resistant to infection with the principal viruses of human hepatitis, in recent years vigorous attempts have been made to transmit types A and B human viral hepatitis to various species of subhuman primates in an effort to overcome this barrier and establish an animal model for studies of experimental hepatitis. One promising development of this research has been the transmission of type A hepatitis to marmosets<sup>6, 7</sup> and type B hepatitis to chimpanzees.<sup>8</sup> However, definitive characterization of hepatitis associated with human types A



and B viruses in either human volunteers or subhuman primates is greatly limited by the inability as yet to isolate and identify the specific viruses. Thus, it cannot be determined with certainty whether the agent which presumably transmitted the disease is identical to that associated with the experimentally induced effects. Evidence is now accumulating that there may be multiple viral agents as yet unidentified (or several variants of the viruses); all capable of causing hepatitis in human or animal models.

Certain aspect of the clinical syndrome of hepatitis have been reproduced in experimental models. For example, in dogs infected with infectious canine hepatitis virus (ICH), the disease occurs in four forms corresponding to similar forms seen in human hepatitis fulminating, severe, mild, subclinical. Anorexia and lethargy are prominent in symptomatic animals, and serum transaminase activities (SGPT; SGOT) increase as they do in patients with hepatitis, concomitant with histologically visible evidence of parenchymal cell damage.<sup>9</sup>

The incubation period, the locus of viral replication, and the period of viremia have been defined in several animal models. Inoculation of mice with virus results in Kupffer cell uptake of the virus, and replication of the virus within these macrophages continues until their capacity to dispose of the virus is exceeded at the end of 3 to 4 days.<sup>10</sup> Only then does viremia develop and parenchymal cells become infected with virus, with clinical symptoms and biochemical evidence of hepatocellular injury occurring at the time of transfer.<sup>11</sup>

It is clear that multiple host -virus factors interact in natural and experimentally- induced infections. It has been demonstrated that the clinical and pathologic manifestations of hepatitis in dogs infected with ICH virus could be distinctly modified by the immune status of the animal,<sup>12</sup> indicating that processes not directly related to viral replication may be implicated in the pathogenesis of prolonged inflammation in partially immune animals.

In humans autoimmune mechanisms are considered important in the pathogenesis of several disease processes. Evidence for liver-specific autoimmunity in the pathogenesis of hepatitis is incomplete at present, although there are reports claiming that a liver-specific immune reaction can be demonstrated to liver extracts on hepato-specific lipoprotein.<sup>13</sup> It is noteworthy that a few patients have been observed with progressive chronic hepatitis coexisting with autoimmune thyroiditis, Sjogren's syndrome, and autoimmune hemolytic anemia, indicating they may have an inherent tendency to develop this form of autoimmunity.<sup>14</sup>

Another group of autoimmune disorders is characterized by the presence of circulating antigen-antibody complexes. These include "collagen" diseases such as systemic lupus erythematosus in which antibodies combined with various cellular components, such as DNA, may be found in the serum. On the other hand, circulating immune complexes which consist of HBAb and HBsAg have been demonstrated in association with cell necrosis in skin, muscle, and articular cartilage. Therefore, it is likely that they mediate certain extrahepatic manifestations (skin rash, myasthenia, arthritis) of type B hepatitis.<sup>15</sup> HBAb-HBsAg immune complexes have not been consistently detected in the liver, so their role in the pathogenesis of either acute or chronic hepatitis is not clearly established.

With regard to T-cell interaction with HB virus, preliminary evidence indicated that T-cell mediated immunity to

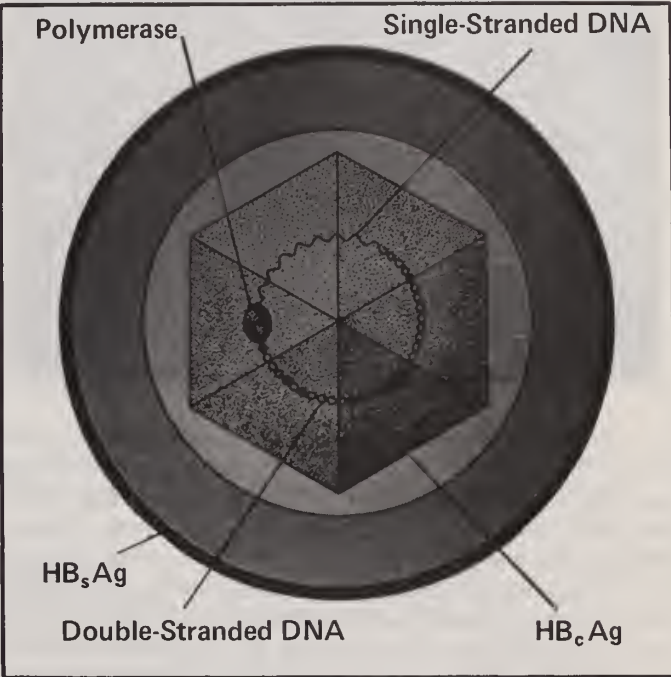
HBsAg may be implicated in the pathogenesis of acute viral hepatitis and chronic active hepatitis.<sup>16</sup>

Hepatitis A virus is a single stranded RNA virus of 27 nm particles uniform in size.

Under electron microscopy serum obtained from patient with hepatitis B infection disclose 42 nm spherical particles (Dane particles) and 20 nm filaments (HBsAg). A schematic representation of the HB virus is depicted in fig. 1.

Non-A, non-B virus has recently been described. It is similar to HB virus, with a DNA nucleoprotein of 37 nm.

Figure 1\*



\* From Ped Annals, May 1977

Clinical Manifestations

The clinical characteristics of acute viral hepatitis are summarized in Table 3. Most cases of hepatitis A are asymptomatic. Among symptomatic children, the first week of illness is characterized by prominent gastrointestinal symptomatology. The morphologic similarity between HA virus and primary enteric viruses suggests that these symptoms may be

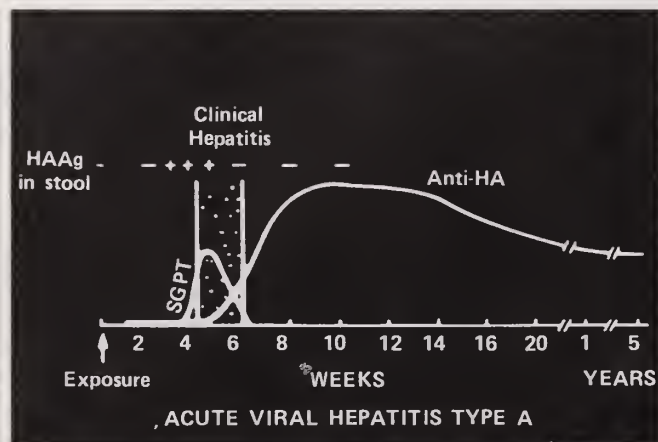
TABLE III

CLINICAL AND EPIDEMIOLOGIC FEATURES OF HEPATITIS A AND B IN CHILDREN		
	Hepatitis A	Hepatitis B
Age and sex	School-age; no sex predilection	Adolescent boys predominantly (probably due to drug abuse)
Spread	Fecal-oral; food and water	Parenteral; blood-oral
Incubation period (days)	14-50	50-180
Onset	Acute with prodrome	Insidious
Icterus period (days)	4-21	12-28
Extrahepatic manifestations	Uncommon	Arthritis, nephritis, urticaria, polyarteritis, serum sickness
Sequelae of chronic disease	Uncommon ( $<2.0\%$ )	More common*
Fulminant course	Rare	Uncommon
Animal model	Marmoset	Chimpanzee
Gamma globulin (GG) prophylaxis	Good; standard GG	Unproved; high anti-HBsAg GG; standard GG

\*Adults show figures of about 10 per cent. No data in children.

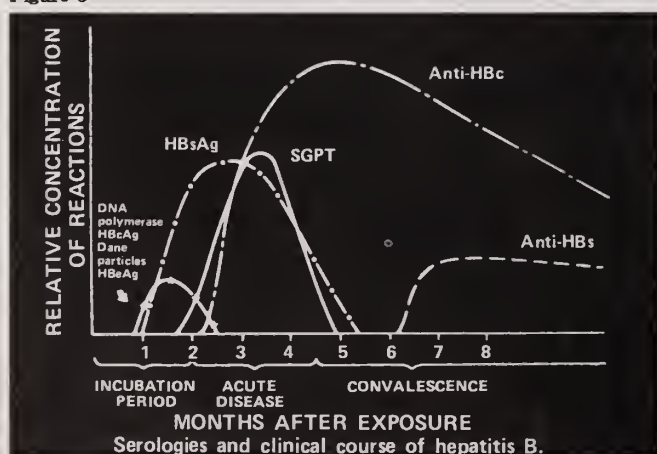
related to HA viral interaction with the mucosa of the intestinal tract. Laboratory tests this time reveal elevated serum transaminase activity, a sensitive indicator of hepatocellular injury and usually the only means of detecting anicteric cases (Fig. 2). Elevations in serum transaminase activity rarely persist longer than 4 weeks. In icteric cases, serum bilirubin elevations, usually not in excess of 15 mg/10 ml, also occur. Fulminant hepatitis and massive hepatic necrosis are seldom seen with hepatitis A infection.

Figure 2



Clinically, type B virus infection is similar to hepatitis A except that the onset of symptoms is usually more insidious and the extrahepatic manifestations such as skin rash, urticaria, joint symptoms, polyarteritis nodosa, pleural effusion, myocarditis, and essential mixed cryoglobulinemia are more prominent. Serum transaminase activity usually reaches peak values about 1-2 months after onset of symptoms<sup>17</sup>. If jaundice is clinically apparent, it usually becomes manifest at the time of peak transaminase activity (Fig. 3). The development of fulminant hepatitis is apparently more frequent with type B disease<sup>18</sup>, but in children ultimate recovery after a 4-6 weeks illness is the outcome in over 90 per cent of patients.

Figure 3



### Diagnosis

In an effort to diagnose patients with type B hepatitis, and also identify carriers at risk of transmitting the disease, a bewildering array of diagnostic tests for the detection of HBsAg and HBeAg have been described. Five frequently

used techniques include in order of decreasing sensitivity: radioimmunoassay (RIA), passive hemagglutination complement fixation, counterimmunoelectrophoresis, and immunodiffusion. The use of these methods to screen blood donors has resulted in a significant reduction in the incidence of post-transfusion hepatitis<sup>19</sup>. Two recently introduced test which provide sensitive indicators of persistent viral replication in the absence of detectable HBsAg, serum DNA polymerase activity<sup>20</sup> and antibody to hepatitis B core antigen (HBcAg)<sup>21</sup> will permit improved clinical identification of patients with hepatitis B.

The electron microscopy assay for hepatitis A antigen and antibody is obviously not a practical routine laboratory procedure. However, the recent development of specific complement fixation and immune adherence tests for hepatitis A antibody<sup>22</sup> provide a more useful method to clinically identify type A disease.

In 1972 Magnus and Espmark described a new group of precipitating antigens—the e antigen (HBeAg)—related to hepatitis B virus infections.<sup>23 24</sup> In later studies the HBeAg was found to be closely related to the presence of circulating Dane particles<sup>25 26</sup> and core-specific DNA polymerase activity<sup>27 28</sup> in serum. The presence of antibody to HBeAg (anti-HBe) has in several studies been correlated with the “healthy” carrier state for HBsAg<sup>29 30</sup> and with low or absent infectivity of serum.<sup>31 32</sup> Early appearance (earlier than two weeks) of anti HBe after the clearing of the HBeAg may indicate an uncomplicated course of the acute hepatitis, whereas a delayed appearance (later than six weeks) might predict a prolonged course including the development of chronic hepatitis.<sup>30</sup>

To further complicate the issue of laboratory diagnosis, several sub types of HBsAg have been described. Although not important from the clinical standpoint, they are useful for epidemiologic purposes (Table 4).

TABLE IV

HBsAg SUB-TYPES	
a y b —	MEDITERRANEAN, NEAR EAST, S. EUROPE, AFRICA
a d w —	N. & C. AMERICA, N. EUROPE
a d r —	S.E. ASIA, FAR EAST
a y r —	KOREA

### Treatment

Uncomplicated acute viral hepatitis is a self-limited disease, and supportive therapy is all the sick patient requires. Limitation of activities and special diets are rarely, if ever, indicated.

In those cases where fulminant hepatic failure supervenes several experimental modalities of treatment have been used with varying success. These include interferone, adenine arabinoside, hemodialysis, plasmapheresis, “total body washout”, animal liver perfusion cross circulation, and charcoal hemoperfusion.



Chronicity of hepatitis B

Ninety per cent of patients with acute hepatitis undergo an uncomplicated course and their hepatic lesions heal. Approximately 8% develop chronic persistent hepatitis. The rest will eventually develop chronic active hepatitis, cirrhosis or liver failure.

Table 5 summarizes the histologic and clinical characteristics of chronic hepatitis.

Typically, these patients have persistence of HBsAg in serum, low anti HBs, high anti HBe (indicative of active viral replication in the presence of HBsAg), elevated SGOT & SGPT, elevated serum immunoglobulins, and HBcAg present.

The risk of chronicity for patients with non-A, non-B hepatitis is 20-40%, while it is non-existent for those with type A infection.

Commercially available human immune serum globulin (HISG) contains significant quantities of hepatitis A antibody. HISG (0.06 ml/kg) should be given to close family contacts, needle stuck or parenterally exposed patients, school outbreaks, and as pre-exposure prophylaxis to those traveling to epidemic area or working with institutionalized patients (dose should be repeated every 6 months if exposure continues).

HISG manufactured after 1972 usually has amounts of antibody to HBsAg sufficient for passive immunization for exposures such as "needle sticks", family contact of acute cases, and newborns of affected mothers (Table 6). Dosages of 0.1 ml/kg or 10 ml (whichever is greater) are recommended as soon as possible after exposure. Whenever possible, the recipient should be checked for circulating HBsAg since antigen antibody complex formation and its sequelae may ensue.

TABLE V\*

HISTOLOGIC AND CLINICAL CHARACTERISTICS OF CHRONIC HEPATITIS		
HEPATIC LESION	MORPHOLOGY	CLINICAL FEATURES
Massive hepatic necrosis (MHN)	Massive necrosis of liver parenchyma with minimal inflammatory reaction. Only portal triads and lobular reticulum framework are preserved.	Rapid onset of mental confusion and somnolence progressing to deep coma; jaundice and fetor hepaticus.
Postnecrotic cirrhosis (PC)	Disruption of lobular architecture with "loss of central veins" (central veins become indistinguishable from portal veins because of proximity); extensive fibrosis; regenerative nodules of variable size.	Onset may resemble acute hepatitis but usually begins gradually with remissions and relapses of malaise, jaundice, ascites, and gastrointestinal symptoms. Ultimately results in hepatic failure.
Subacute hepatitis with multi-lobular necrosis (SHMN)	Total destruction of several contiguous lobules with widespread hepatocyte necrosis and variable infiltration of lymphocytes and plasma cells. In these areas portal tracts are drawn together. In other areas the lesions of SHBN or CAH may be seen.	May present acutely, or occur in the course of CAH and SHBN. Remissions and exacerbations of malaise, jaundice, ascites. Most patients developed cirrhosis, some (25 % in one study) show improvement to CPH while on treatment.
Subacute hepatitis with bridging necrosis (SHBN)	Parenchymal necrosis with mainly lymphocytes and plasma cell infiltration involving contiguous lobules. Zones ("bridges") of necrosis, inflammation and fibrosis extend between portal areas, and between portal areas and central veins. May have areas of CAH.	May develop during acute hepatitis or follow CAH. The lesion signifies persistent liver disease; in one study, 20 % of patients on treatment improved to CPH.
Chronic active hepatitis (CAH)	Infiltration of portal tracts with lymphocytes, plasma cells and histiocytes. Inflammation extends into parenchyma with "piecemeal necrosis": a spilling over of portal inflammatory cells into the surrounding parenchyma with necrosis of hepatocytes at the lobular periphery. Features of acute hepatitis with centrilobular hepatocyte necrosis may be present.	Frequently present de novo but may occur in the course of SHMN, SHBN, CPH or follow acute hepatitis. Intermittent course of anorexia, jaundice, abdominal pain, pruritus. Female predominance (75 to 80 %). Elevated immunoglobulins; autoantibodies prominent in serum. Ultimate prognosis poor but prolonged remissions induced by steroids in most patients.
Chronic persistent hepatitis	Infiltration of portal tracts with chronic inflammatory cells, preserved lobular architecture with minimal inflammation, little or no fibrosis and minimal necrosis.	In general, a benign course of prolonged hepatitis with eventual recovery.
Carrier (HBAG)		Apparently healthy. Represent reservoirs for transmission of Type B hepatitis.

\* From Ped Annals, May 1977

Immunoprophylaxis

Passive Immunization

Passive immunization to protect contacts or hepatitis A is now well established.<sup>33</sup> It is not certain that in the open community active-passive immunity occurs, as has been reported in such closed settings as schools and army camps.

High-titer HBs antibody HISG (HBIG), which has been more successful in passive protection, is now commercially available.

The elimination of commercial blood and the diligent screening of blood donors can dramatically reduce the incidence of hepatitis B via blood transfusions. A number of studies suggest that regular HISG significantly reduces the

incidence of non-A non-B post-transfusion hepatitis.<sup>34</sup> It is not clear that immunotherapy has any advantage over the basic prophylactic measures mentioned above.

TABLE VI

## H. B. V. IMMUNOPROPHYLAXIS

## CONTACTS OF ACUTE HBV PATIENT

1. Sexual contact 0.06 ML/KG HBIG
2. Needle or parenteral contact  
0.06 ML/KG HBIG
3. Newborn infant 0.13 ML/KG HBIG
4. Pre-exposure Immunoprophylaxis

## NOT RECOMMENDED

IF HBIG Not available

- |                   |            |     |
|-------------------|------------|-----|
| 1. Sexual contact | 0.12 ML/KG | ISG |
| 2. Needle contact | 0.12 ML/KG | ISG |
| 3. Newborn infant | 0.5 ML/KG  | ISG |

## Active Immunization

The safety and efficacy of a hepatitis B formalin-inactivated vaccine have been established in chimpanzees and humans<sup>35</sup>. Preliminary results using the formalin-activated vaccine as well as a heat-inactivated one and ultrapurified subparticles are encouraging, but the ultimate conclusions about safety, potency, and protective capacity have yet to be established.

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# Presentación de Casos

## Sinus Node And Atrial Dysfunction During Hypercalcemia

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Charles D. Johnson, MD, FACC

**Abstract:** A patient who demonstrated sinoatrial node dysfunction and atrial arrhythmias secondary to marked hypercalcemia is reported. A temporary pacemaker was required. An atrial pacing study was done during a serum calcium level below 12 mg/dl, the results of the study were normal. A cystic parathyroid adenoma was surgically removed. The effects of hypercalcemia on the heart and electrocardiogram are reviewed.

Sinoatrial node dysfunction and atrial arrhythmias secondary to severe hypercalcemia have been rarely documented. We wish to report a patient who demonstrated such arrhythmias during severe hypercalcemia of hyperparathyroidism, who required temporary cardiac pacemaker placement.

### Brief Clinical History

This 48-year-old female was admitted to University Hospital on 12-29-81, because of headaches, irritability, anorexia, nausea, vomiting, constipation, epigastric pain, weight loss, polyuria, nocturia and polydipsia. There was a past history of renal calculi, and hypertension for many years. An extensive evaluation was performed. Medical and subsequently surgical therapy were practiced. See figures 1-3.

Figure 1

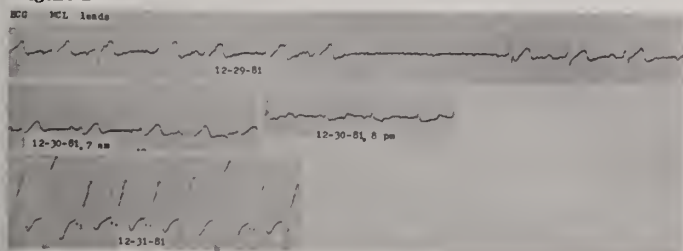


Fig. 1. 12-29-81 (Top) ECG-CCU Monitor tracing on admission day. Serum Calcium - 18.1 mg/dl. Followed by a precordial V<sub>1</sub> tracing at 7 AM and a Lead 2 tracing at 8 PM. The L<sub>2</sub> tracing demonstrated coarse atrial fibrillation. A temporary pacemaker was placed on right ventricular apex, but it moved to the right ventricular outflow tract (bottom, 12-31-81). Refer to context for complete ECG description.

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Figure 2

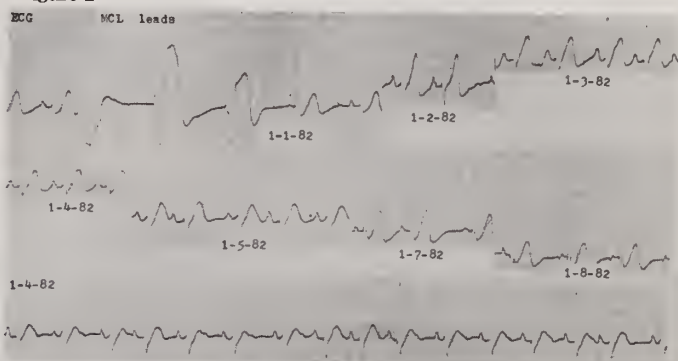


Fig. 2. ECG-CCU Monitor tracing from 1-1-82 to 1-8-82. The serum calcium were fluctuating between 12.8 to 15.1 mg/dl. Refer to context for ECG description.

Figure 3

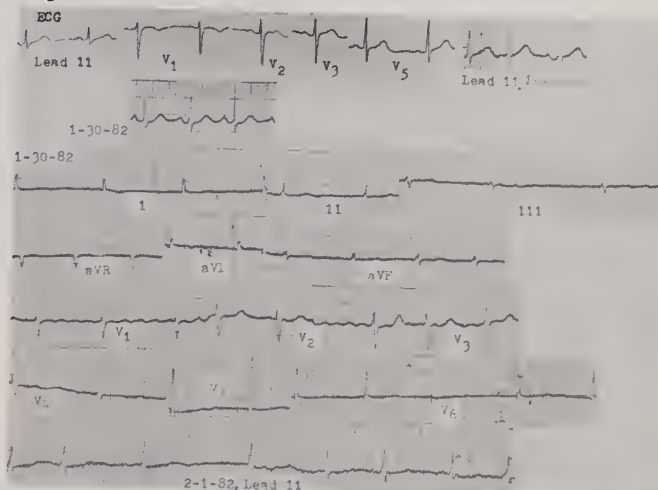


Fig. 3. 1-29-82 (Top) ECG tracing taking in the Recovery Room after parathyroid cystic adenoma remotion. Serum calcium was 8.9 mg/dl. On day 30, there is atrial fibrillation. On 2-1-82 a trace revealed similar atrial fibrillation.

CCU - Coronary Care Unit  
ECG - Electrocardiogram

### Description of Electrocardiograms (ECG)

A complete ECG done in the Emergency Room on 12-29-81 (not illustrated) showed an electrical axis of -20, T wave changes and findings similar to those illustrated below.

Figure 1. 12-29-81. Serum calcium (Ca) 18.1 mg/dl, phosphorus (P) 2.6 mg/dl, serum potassium (K) 3.1-3.4 meq/L, blood urea nitrogen 28 mg/100 ml, creatinine 3 mg/100 ml. Q-T interval 0.38 seconds (S), QaT 0.30 S.; variable P wave morphology and irregular ventricular rhythm; the third QRS complex may be a nodal escape beat. Thereafter, paroxysmal sinoatrial block, arrest, atrial standstill, for about 3 cycles, occur compatible with Type II-Sick Sinus Syndrome; variably prolonged P-R intervals and P contours occur afterwards. 12-30-81. Ca 17.6-18.7, P 1.2, K 3.3-3.7.

At 7 A.M. similar variability is present. At 12 noon, the pulse was 60, but at 12:12 P.M., because of sinoatrial block, a temporary pacemaker was placed. The catheter was looped in the right ventricle but continued to pace and sense. Atrial flutter (AF)/atrial fibrillation (Af) were present at 8 p.m. On 12-31-81, there was an artificial pacemaker rhythm, rate 100 per minute; the Spike-aT interval was 0.24 S.

Figure 2. 1-1-82 to 1-8-82. Ca 12.8-15.1, P 1.7. Q-T 0.28-0.33 S., QaT 0.20-0.24 S. The pattern is similar to that in Figure núm. 1; the P-P and R-R cycles are variable. In the strip of 1-1-82, there is a premature ventricular beat (PVC) followed by 2 pacemaker escape beats at a rate of 61-62, and then a nodal escape beat. On 1-10-82, the Ca was 20 but no ECG was obtained. These arrhythmias suggest the diagnosis of chaotic or multifocal atrial rhythm (vide infra).

On 1-19-82, Atrial pacing revealed normal sinus and atrioventricular (AV) node function; Wenckebach block occurred at a pacing rate of 130; the atropine response was normal and there was no carotid sinus hypersensitivity. the serum calcium was 12 mg/dl. On 1-29-82, a cystic parathyroid adenoma was removed. Diagnosis: Primary Hyperparathyroidism with Hypercalcemia.

Figure 3. The initial top strips showed a normal ECG. 1-29-82. Ca 8.3-12.7, P 3.4, P waves variable. On 1-30-82 (second row) the rate was variable, approximately 112. A complete ECG of 1-30-82 (Ca 9.7, P 2.3) showed an axis of +12, T wave abnormalities and AF/Af with low voltage "f" waves and a minimal rate of 33. On 2-1-82, (Ca 8.3, P 2.5, K 4.5, Bun 11 mg/100 ml), a trace revealed similar Af. On 5-7-82, the Ca and P were normal.

## Discussion

### Electrocardiogram

The earliest and probably most common electrocardiographic finding in hypercalcemia is shortening of the Q-T interval. The ST segment becomes shorter or disappears, or it may be depressed without upward concavity. The sharp upstroke of the ascending limb of the S wave merges with the ascending limb of the T. The T wave may be less peaked (Ca 16 mg/dl) or gradually widen (16 mg/dl) with broad rounding of the T wave, whose frontal axis may shift. Inversion of TII and TIII can occur. There is a fair correlation between hypercalcemia and the Q-TC, better with the QOTc (Q to onset of T) and best with Qat (Q to apex of T) intervals, although studies are not consistent. U waves may develop and be normal or prominent.<sup>1-6</sup>

### AV and Intraventricular Block

QRS complexes may be slightly prolonged, showing a slurred rSR in lead V<sub>1</sub>. At extreme hypercalcemia first degree and even second or third degree AV block can occur, and infrequently QRS prolongation, i.e. right bundle branch block. Crum observed reversible Wenckebach phenomenon Ca 15.3 mg/dl, attributed to excessive vagal action induced by the hypercalcemia. Ginsberg observed complete heart block in a case with Ca of 15.8 mg/dl and a ventricular escape rate of 40, which subsequently changed to 2:1 AV block and then to normal.<sup>1-3-6-11</sup>

### Cardiac Arrhythmias

Cardiac arrhythmias are uncommon, but various arrhythmias have been reported, particularly at extremely high

levels of hypercalcemia (hypercalcemic crisis, 16 mg/dl). The critical toxic level is 16-18 mg/dl. There is no correlation with heart rate but acute hypercalcemia may induce bradycardia. Sinus tachycardia occurs (Ca 14.3) and atrial premature contractions. Atrial fibrillation (Af) has rarely to infrequently been seen, perhaps due to the associated atherosclerotic heart disease.<sup>2 3 10 12</sup> Lischer<sup>13</sup> reported atrial flutter and heart block (apical rate 160) in a patient with parathyroid crisis (Ca 19 mg/dl). Jennings et al<sup>14</sup> noted hypotension, nodal rhythm and questionably related sudden death post-operatively in a patient with a Ca of 18 mg/dl. Premature ventricular contractions (PVC), ventricular tachycardia (VT) and fibrillation (Vf) have been observed. Sudden death may be related to Vf as seen in hyperparathyroidism and digitalis toxicity.<sup>6 15</sup>

Voss and Drake<sup>3</sup> documented reversible multiple arrhythmias and AV block (due to excess vagal action of direct toxic effect of the calcium) in a patient with parathyroid adenoma and a Ca of 11.2-13.6 mg/dl, P 1.5-1.8 mg/dl. This comprised: episodes of sinus arrest followed by nodal escape beats and a ventricular rate as low as 15 per minute, intermittent first degree AV block (P-R interval up to 0.26 S), bouts of paroxysmal Af, sinus bradycardia and shortened ST segment. A pacemaker was employed during the surgery.

Varying grades of second degree AV block with episodes of arrest were observed during therapy with digitalis and procainamide in another case.<sup>10</sup>

Hypercalcemia mimics digitalis, and the two may be synergistic predisposing to digitalis intoxication and possibly sudden death. Intravenous (IV) Ca to a digitalized patient during resuscitation, or rapid administration of digitalis to a hyperparathyroid hypercalcemic patient may induce bradycardia, extrasystoles, varying AV block and cardiac arrest.<sup>3 6 10 12</sup>

In humans, transient sinus bradycardia, sinus arrest and block, shifting of the pacemaker, PVCs, VT, Vf, varying degrees of heart block, flattening and inversion of T and P waves occurred during rapid IV injections of Ca solution. Sinoatrial and AV block and arrhythmias have also been produced by Ca injections in dogs.<sup>2 16-18</sup>

Long-standing hypercalcemia may predispose to calcification in the myocardium, large and medium-size blood vessels and other soft tissues. AV block may be due to scattered subendocardial petechiae, myocardial calcification and focal myocardial necrosis. Hypertension, idiopathic hypertrophic subaortic stenosis and supra-aortic stenosis are related to hypercalcemia.<sup>19</sup>

### Electrophysiology

Hypercalcemia is characterized by: 1) a decreased duration of phase 2 and of the action potential (AP) - shortening of recovery time and refractory period; however, the shape and amplitude of the AP and the resting potential may hardly be changed; 2) shortening of mechanical ventricular systole; 3) slight decrease in activation velocity with a decreased conduction velocity; 4) a slight increase in spontaneous diastolic depolarization with questionable effect on automaticity; myocardial automaticity may be reduced; 5) augmentation of excitability threshold potential or a less negative threshold potential; 6) hyperpolarization of sinoatrial node cells; 7) production of a spastic contraction of the heart. It is stated that hypercalcemia never markedly alters cardiac functions.<sup>6 12</sup>



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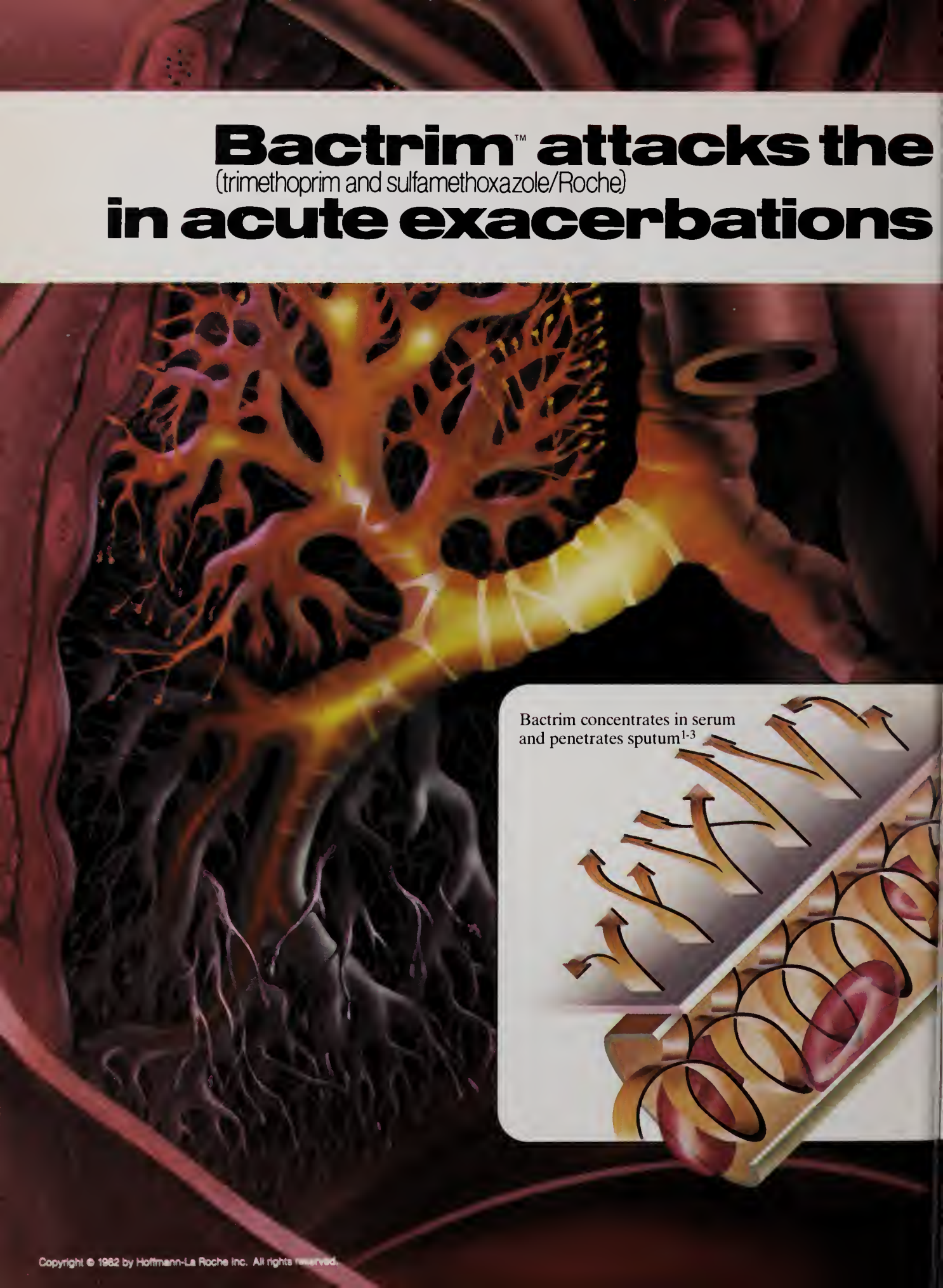
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# major pathogens of chronic bronchitis\*

## Bactrim clears sputum of susceptible bacteria

In sputum cultures from patients with acute exacerbations of chronic bronchitis, *H. influenzae* and *S. pneumoniae* are isolated more often than any other pathogens.<sup>4,5</sup> One study of transtracheal aspirates from 76 patients with acute exacerbations found that 80% of the isolates were of these two pathogens.<sup>5</sup>

Bactrim is effective *in vitro* against most strains of both *S. pneumoniae* and *H. influenzae*—even ampicillin-resistant strains. And in acute exacerbations of chronic bronchitis involving these two pathogens, sputum cultures taken seven days after a two-week course of therapy showed that Bactrim eradicated these bacteria in 91% (50 of 55) of the patients treated.<sup>6</sup>

## Bactrim reduces coughing and sputum production

In three double-blind comparisons with ampicillin *q.i.d.*, Bactrim DS proved equally effective on all clinical parameters.<sup>7,9</sup> Bactrim reduced the frequency and severity of coughing, reduced the amount of sputum produced and cleared the sputum of purulence.

Bactrim has the added advantages of *b.i.d.* dosage convenience and a lower incidence of diarrhea than with ampicillin, and it is useful in patients allergic to penicillins.

Bactrim also proved more effective than tetracyclines in 10 clinical trials

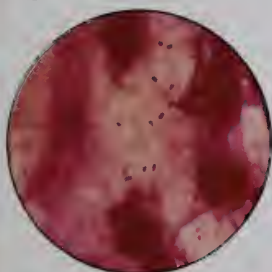
involving nearly 700 patients.<sup>10</sup> Overall clinical condition of the patients, changes in sputum purulence, reduction in sputum volume and microbiological clearance of pathogens—all improved more with Bactrim therapy than with tetracyclines. G.I. side effects occurred in only 7% of patients treated with Bactrim compared with 12% of tetracycline-treated patients. (See Adverse Reactions in summary of product information on next page.)

Bactrim is contraindicated in pregnancy at term and nursing mothers, infants under two months of age, documented megaloblastic anemia due to folate deficiency and hypersensitivity.

Bactrim DS. For acute exacerbations of chronic bronchitis in adults\* when it offers an advantage over single-agent antibacterials.

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attacks *H. influenzae*—even  
ampicillin-resistant strains



attacks *S. pneumoniae*



## Economical b.i.d.

# Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole/Roche)

\*Due to susceptible organisms. Please see next page for summary of product information.

# Bactrim™

(trimethoprim and sulfamethoxazole/Roche)

Before prescribing, please consult complete product information, a summary of which follows:

**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. *Note:* The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

**For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials.** To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.

**For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.**

**For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.**

**Also for the treatment of documented *Pneumocystis carinii* pneumonia.**

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term, nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age.

**Warnings: BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL**

**PHARYNGITIS.** Clinical studies show that patients with group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hemopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions: General:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin; reassess coagulation time when administering Bactrim to these patients.

**Pregnancy: Teratogenic Effects:** Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folic acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea, pseudomembranous colitis and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage: Not recommended for infants less than two months of age.**

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN**

**Adults:** Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

**Children:** Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

**For patients with renal impairment:** Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

**ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS:**

**Usual adult dosage:** 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 14 days.

**PNEUMOCYSTIS CARINII PNEUMONITIS:**

**Recommended dosage:** 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100; Prescription Paks of 20 and 28 Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40 Pediatric Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); cherry flavored—bottles of 100 ml and 16 oz (1 pint). Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); fruit-licorice flavored—bottles of 16 oz (1 pint).



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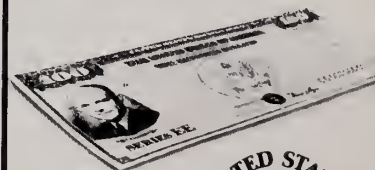
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Differential Diagnosis

Sex, age and heart rate of the patient, drugs, myocardial disease, ischemia, congestive heart failure and other electrolytes such as potassium, may bear on the electrocardiographic manifestations. Hypercalcemia is a pharmacologic antagonist to the cardiac effects of hyperkalemia, but it often enhances cardiac arrhythmias.<sup>5 6</sup>

Sinoatrial node dysfunction, as this patient demonstrated, has been rarely documented in clinical hypercalcemia.<sup>3 10</sup> The atrial arrhythmia reveals some features of wandering atrial pacemaker and multiple atrial premature beats. However, it may best be categorized as Chaotic or Multifocal Atrial Rhythm, Dysrhythmia of Mechanism. The latter has been regarded as an extreme variant of a wandering atrial pacemaker with atrial premature beats.<sup>20-23</sup> AF/Af may be a manifestation of hypercalcemia and the Sick Sinus Syndrome. But when it recurred post-operatively in the patient the serum calcium was normal.

**Resumen:** Se reporta el caso de un paciente que desarrolló disfunción del Nodo Seno-Atrial debido a hipercalcemia severa. Se necesitó un marcapaso temporero para su manejo. El paciente fue sometido a un rastreo atrial cuando los niveles de calcio sérico bajaron de 12 mg/dl, el estudio fue normal. Un adenoma quístico paratiroideo fue removido quirúrgicamente. Se repasan los efectos de la hipercalcemia sobre el corazón y la electrocardiografía.

Acknowledgement

The authors wish to thank Arleen López for the typing of the manuscript.

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# ARTICULOS ESPECIALES



## *New American College of Radiology Guidelines on Mammography*

**M**ammography has made highly significant contributions in the detection of breast cancer in symptomatic women at any age, and in the screening of asymptomatic women 50 years of age or older. However, screening mammography in women under age 50 is less clearly established because of the lack of supporting data from controlled randomized studies and hypothetical projections of radiation risk.

The bases for these concerns about screening mammography in women under age 50 are:

1. The data from the breast screening (physical examination and mamography) project of the Health Insurance Plan (HIP) of Greater New York in the early 1960's revealed identical mortality for the study group (those screened with physical examination and mammography) and the control group (no screening) for women under 50 years of age. There was no separate assessment of physical examination versus mammography. However, very few cancers were found by mammography in this age group.

2. The report increased incidence of breast cancer in: a) women exposed to the atomic bombs in Japan at the end of World War II; b) women exposed to varying amounts of fluoroscopy during the management of tuberculosis; c) women with post-partum mastitis treated with radiation therapy; and d) a series of Swedish women who received high dose x-ray therapy for benign disease.

3. The Committee on Biological Effects of Ionizing Radiation (BEIR) of the National Academy of Sciences has indicated that the risk of low doses of radiation causing breast cancer is small, but they have speculated that it may never be zero (the possibility of zero is not excluded by the data). This is based upon extrapolation from high radiation dose data (low dose data are lacking). Considerable disagreement exists concerning these conclusions.

However, in response to these concerns:

1. Results from screening at the 27 ACS-NCI Breast Cancer Detection Demonstration Project (BCDDP) in the

late 1970's indicate that approximately one-third of the breast cancers occurred between the ages of 35 and 50 and that most of these lesions were either in-situ or did not involve the regional lymph nodes. Most of these cancers were detected by mammography and a much higher percentage were detected by mammography alone than by physical examination alone.

2. There has been progressive and significant improvement in the quality and diagnostic accuracy of optimum mammography and there has been marked reduction in radiation dose (this should not exceed one rad at the mid-breast with a two view examination).

3. While the risk of irradiation from optimum mammography is immeasurably small at all ages, the linear, no threshold response model seems to be a conservative method for estimating population risk for women under the age of 40. However, the available data strongly suggest that the risk for breast cancer induction by radiation is much smaller, if it exists at all, for women over age 40 at the time of initial exposure.

This improved mammographic ability to detect many small breast cancers, particularly in women aged 40-50, strongly suggests that substantially favorable benefit/risk ratios will apply to all women over forty years of age, so long as optimum mammographic technique and carefully monitored equipment are used.

These guidelines are proposed as a summary of current informed opinion:

### Introduction

- 1) Mammography and physical examination are clearly complementary procedures and the end results are materially improved when the two diagnostic procedures are optimally combined. However, it is a basic tenet of cancer diagnosis and treatment to detect the primary tumor when it is small or nonpalpable and mammography, appropriately performed, is the most effective non-invasive diagnostic tool for those purposes.

- 2) Although the presumed risks of radiation at current optimum levels of exposure (less than 1 rad to the midbreast for a two view examination) are immeasurably small, continued efforts to reduce exposure should be made. However, this should not be at the expense of image quality which must be preserved to insure the best benefit-risk ratio.

- 3) Optimum and reproducible image quality are essential for accurate mammography interpretation. If xeromammography is the method of choice, it should be performed



with a tungsten target tube and breast compressions during the x-ray exposure. If film-screen mammography is the method of choice, it should be performed only with an x-ray unit specialized for mammography. Each radiologist should have periodic monitoring of his equipment and procedures to assure that the patient's radiation exposure is being maintained at the lowest feasible level (less than 1 rad at the mid-breast for a two view examination) consistent with this optimum image quality.

4) At present, other imaging modalities such as thermography and ultrasound have not demonstrated the requisite sensitivity to substitute for mammography in screening or diagnosis. The presumed risks of radiation with mammography are not a justification for their use. Computerized tomography has had limited application, requires greater radiation exposure, and has some risk of adverse reaction to the intravenous injection of contrast. There is active research going on with these and a number of other imaging modalities.

### Care of Women with Symptoms

Mammography is an essential part of the evaluation of the patient and when optimally combined with physical examination, offers a high degree of accuracy.

Since the incidence of naturally occurring breast cancer is considerably higher in symptomatic women, the higher yield of non-palpable cancers results in even greater benefit-risk than in asymptomatic women.

### Screening of Asymptomatic Women

1) These recommendations for periodic screening mammography of women under age 50 are made because of accumulating data on benefits and the lead time gained by earlier detection. The American College of Radiology believes that these recommendations represent the most prudent advice based upon the best currently available evidence.

2) All women should be taught proper breast self-examination by age 20 and should have an annual examination of the breast after age 35.

3) The first, or baseline, mammograms should be obtained by age 40. An earlier age is preferable when there is a personal history of breast cancer or a history of premenopausal breast cancer in the patient's mother and/or sisters.

4) Subsequent mammographic examination should be performed at one to two year intervals determined by the combined analysis of physical and mamographic findings and other risk factors, unless medically indicated sooner.

5) Annual mammography and physical examination are recommended for all women over age 50.

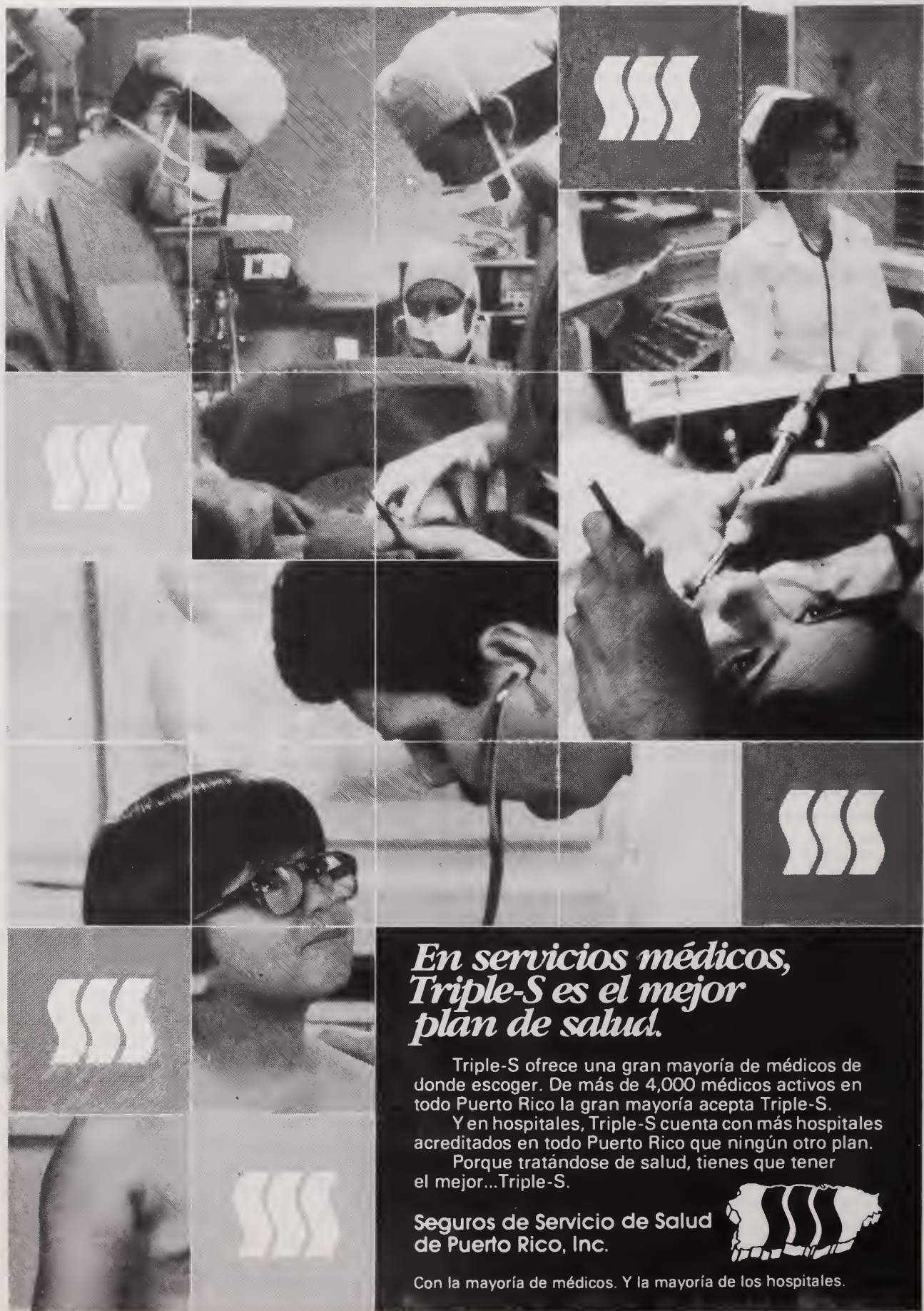
### Research Programs

Screening mammography of asymptomatic women 40-50 years of age can detect significant numbers of nonpalpable or minimal breast cancers and this indicates that a favorable benefit-risk assessment will be obtained. Nevertheless, research must be continued and encouraged to:

- 1) Obtain more data from controlled studies;
- 2) Improve methods for measurements of low level radiation;
- 3) Further reduce radiation dose in mammography consistent with good image quality;
- 4) Determine the most appropriate age at which to begin screening for different risk groups;
- 5) Define women a high risk;
- 6) Establish the appropriate intervals for re-examination;
- 7) Define those mammographic findings that dictate the examination at a shorter interval;
- 8) Collect additional evidence on the benefits and risks of mammography;
- 9) Provide continuing education and training for radiologists and technologists, and current information for other physicians and patients regarding the role of mammography and other breast imaging procedures.

### Future Statements

The guidelines are based on current available information. They will be revised when further information dictates and/or when more is learned about the control of breast cancer.



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## Ambulatory Surgery: When and What Procedures

In 1979, the National Capitol Medical Foundation (NCMF), a Washington, DC, professional standards review organization (PSRO), listed 51 surgical procedures that had to be done in an outpatient setting to be eligible for Medicare or Medicaid reimbursement. The foundation's list marked the beginning of what has become a national trend in the health-care field.

Since 1979, a few state departments of health, other PSROs, several state Blue Cross and Blue Shield plans, and recently the U.S. Department of Health and Human Services (HHS) have published similar lists of surgical procedures. In addition, some groups offer financial incentives to physicians who perform certain procedures in their offices. Although private insurance companies are encouraging their subscribers to use outpatient facilities whenever possible, Neil Swan, Washington spokesperson for the Health Insurance Association of America, said "By and large, companies have not developed lists of specific procedures approved for the outpatient setting." Like a few other large companies, the Pillsbury Company, located in Minneapolis, has a self-administered medical plan for its employees. "We are considering incorporating a list of ambulatory surgical procedures into our medical plan," said Tim Temple, director of health care at Pillsbury. "When possible we want to avoid hospital room and board charges," he said.

The lists are part of a larger effort to contain health-care costs by encouraging physicians to use outpatient services whenever possible. NCMF identified five conditions for which reimbursement would be provided even if the selected procedures are performed on an inpatient basis:

- Presence of medical conditions that make prolonged post-operative observation by a nurse or skilled medical personnel a necessity, such as, heart disease or severe diabetes.
- If an unrelated procedure that requires hospitalization is being done simultaneously.
- Lack of proper home post-operative care.
- If another surgical procedure could follow the initial procedure, such as, one-stage breast biopsy followed by a mastectomy.
- Technical difficulties, documented at the time of admission or by operative notes.

All of the groups that have issued lists make allowances for patients who may require hospitalization because of a concurrent medical condition.

HHS expects the expanded ambulatory surgery benefits to save the federal government \$2-million in fiscal year 1983. HHS's list of 96 surgical procedures was issued on August 5 in conjunction with final regulations implementing section 934 of the 1980 Omnibus Reconciliation Act (Public Law 96-499). Under the regulations, which became effective on September 7, both independent and hospital-affiliated ASCs

were eligible for Medicare reimbursement, which was limited to 80 percent.

### Access to services

Although the College supports the concept of ambulatory surgery as a means of cutting health-care costs, it has expressed concern over development of lists of specific surgical procedures. "We believe that categorizing disparate procedures unequivocally as 'ambulatory' does not take into account patient suitability or give proper weight to surgical judgment," ACS Director, Dr. C. Rollins Hanlon, said in a letter dated June 19, 1981 to Carolyn K. Davis, PhD, administrator of the Health Care Financing Administration (HCFA). Dr. Hanlon's letter was written in response to HCFA's formal request for comments on the then proposed regulations. "It would seem that any restriction of patient access to the adjudged safety of inpatient settings would scarcely be desirable from either the medical or financial standpoint," Dr. Hanlon said.

The degree to which the lists are used to restrict access to inpatient services differs among the various groups that have issued lists. While some insurers use the lists simply to make physicians more aware of the kinds of procedures that can be done on an outpatient basis, others will not reimburse hospital inpatient costs unless physicians prove that their patients' medical conditions make inpatient services necessary.

Blue Shield of California, which has issued a list of 700 procedures, falls into the former group of insurers. When reimbursing claims, the California plan does not consider the settings in which surgical procedures were performed. However, after payment is made, all insurance claims that involve one of the 700 selected procedures are reviewed to ensure that the physicians who used inpatient services had valid medical reasons for treating the patient in a hospital. If a physician persists in hospitalizing patients without valid medical reasons, the California plan will report the physician to a local peer review board, but it will not refuse to reimburse hospital costs.

Similarly, last year Blue Cross and Blue Shield United of Wisconsin identified 33 procedures that it has been encouraging physicians to perform in ambulatory surgery centers. However, within the next year, says Leo E. Suycott, president of the Wisconsin plan, the plan will begin to offer its subscriber groups an insurance option requiring physicians to obtain the plan's approval before admitting a patient to a hospital for any of the 33 selected procedures. "If only ten percent of the high-frequency cases are shifted to the outpatient setting," Suycott said, "we will save our subscribers around \$3-million annually."

The Blue Shield and Blue Cross Plan of Minnesota already offers this option to its subscriber groups. Under the group plan, physicians must document a medical need for inpatient services before hospitalizing patients for any of the procedures that have been listed as ambulatory. If the plan's medical staff finds that a physician's reasons for requesting inpatient services are inadequate, the physician is given 30 days to provide adequate documentation. Although the plan does not include a specific definition of what constitutes a medical need for inpatient services, Ronald Osborne, vice president of health service research at the Illinois plan, claims, "It's fairly obvious when physicians do not provide adequate documentation."

## Specific Conditions

When Medicaid recipients in Maryland elect to have any of 65 selected surgical procedures performed on an inpatient basis, the admitting physicians must contact the Maryland Department of Health and Mental Hygiene and explain why the patient requires inpatient services. Otherwise, the hospital will not be paid for inpatient services; instead it will be paid an amount equivalent to what would be paid for outpatient services. The Wisconsin Bureau of Health Care Financing employs a similar system of reimbursing hospitals for Medicaid costs. The Bureau has identified 21 procedure groupings as ambulatory surgery procedures. However, unlike the Maryland health department and most Blue Cross and Blue Shield associations, the Wisconsin bureau has identified criteria that may justify the use of inpatient services for any of the surgical procedures that have been identified as ambulatory.

According to Alan Dann, reimbursement analyst for the Wisconsin health bureau, both diagnostic information and related medical services information are used to determine whether a need for inpatient services exists. The Wisconsin health bureau has captured this information in their claims-processing computer. If the health bureau determines that a need does not exist after a procedure has been done on an inpatient basis, the hospital will only be reimbursed for the cost of a one-day hospital stay. By next spring, the Wisconsin health bureau will introduce an incentive program to encourage physicians to use ambulatory surgery settings. Under the new program, physicians who perform any of a group of selected procedures in an ambulatory surgery center will be paid a standard amount. However, if any of the

The list of procedures covered under HHS's expanded Medicare Part B program for ambulatory surgical centers was printed in the August 5, 1982, issue of the *Federal Register*. HHS has classified the procedures into four reimbursement groups according to complexity and cost: Group 1-\$231, Group 2-\$275, Group 3-\$296, Group 4-\$336.

### Integumentary System

#### **Group 1**

Benign lesion, excision (lipoma)  
Fingernail, Toenail removal  
Malignant lesion, excision (Basal cell, Melanoma)

#### **Group 3**

Breast biopsy (incision, excision uni-or bilateral)  
Mandible cyst excision, simple  
Pilonidal cyst excision, simple  
extensive  
Skin graft

#### **Group 4**

Gynecomastia excision, uni- and bilateral

### Musculoskeletal System

#### **Group 1**

Closed reduction of nasal fracture  
Tenotomy, hands, fingers, ankle, feet and toes-Trigger finger release (tendon sheath, incision for)

#### **Group 2**

Phalangectomy (amputation, fingers and toes)  
Sequestrectomy  
Tendon sheath release (De Quervains)  
Zygoma (Zygomatic arch) reduction

#### **Group 3**

Bursectomy  
Capsulectomy/capsulotomy metacarpophalangeal and interphalangeal)  
Ganglionectomy (wrist)  
Neuroma excision (Morton's and cutaneous and digital nerves)  
Osteotomy metatarsal (metatarsal head excision)  
Tendon repair without graft, implant or transfer

#### **Group 4**

Hammertoe repair  
Boutonniere repair  
Bunionectomy  
Ligament repair  
Neurectomy  
Osteotomy  
Synovectomy  
Arthroscopy  
Fasciectomy/Fasciotomy  
Arthrodesis  
Arthroplasty  
Tendon repair with graft, implant or transfer

### Respiratory System

#### **Group 1**

Bronchoscopy  
Excision turbinate  
Laryngoscopy

#### **Group 2**

Nasal polypectomy  
Antral window (puncture) (Sinusotomy)

#### **Group 3**

Ethmoidectomy

#### **Group 4**

Septal reconstruction  
Submucous resection (turbinate and nasal septum)

### Cardiovascular System

#### **Group 1**

Temporal artery, ligation or biopsy

#### **Group 4**

Varicose vein ligation

### Hemic and Lymphatic System

#### **Group 2**

Cervical node (lymph node) biopsy

### Digestive System

#### **Group 1**

Esophagoscopy  
Gastrosocopy  
Rectal dilation  
Tongue biopsy

#### **Group 2**

Branchial arch appendage excision  
Liver biopsy, percutaneous  
Vermilionectomy (lip peel)  
Fistulectomy



services are performed in a physician's office, the physician will receive an additional amount equivalent to two hospital visits. Conversely, if the procedure is performed on an inpatient basis, this additional amount may be deducted from the standard amount that the physician would have normally received.

Most physicians and insurers agree that using outpatient services rather than inpatient services is less costly; however, some groups have identified 700 ambulatory surgical procedures, while others have cited only 21. The Wisconsin health bureau has established parameters which may justify using inpatient services, but most groups prefer to evaluate each case individually. Exactly what procedures can be safely performed on an outpatient basis and exactly what medical conditions justify using inpatient services remain unsettled questions.

To date, insurers have been the strongest proponents of developing lists of surgical procedures. Nevertheless, Robert C. Williams, executive director of the Free-standing Ambulatory Surgical Association in Phoenix, believes that private businesses will become "the aggressive entity dictating to providers and insurers what they want done and where they want it done."

NOTA EDITORIAL: Por considerarlo de interés para las especialidades quirúrgicas reproducimos este artículo según apareció en el *Bulletin of the American College of Surgeons*. Vol. 67 (11): 21, 1982.

### **Group 3**

Colostomy revision (simple)  
Wedge resection of lip  
Hemorrhoidectomy

### **Group 4**

Peritoneoscopy (mini-laparotomy)  
Herniorrhaphy

### Urinary System

#### **Group 1**

Cystourethroscopy  
Urethral dilation

#### **Group 3**

Transurethral resection of bladder tumor (Cystourethroscopy w/operative procedure)

### Male Genital System

#### **Group 1**

Prostate biopsy

#### **Group 2**

Orchiectomy

#### **Group 3**

Hydrocele excision  
Spermatocele excision

#### **Group 4**

Varicocele repair

### Female Genital System

#### **Group 1**

Vulva (labia) biopsy  
Examination under anesthesia (pelvic)

Vaginal stenosis release (dilation of vagina under anesthesia)  
Culdoscopy (Culdocentesis)

#### **Group 2**

Hysterosalpingogram  
Perineoplasty  
Vaginal tumor (cyst) excision

#### **Group 3**

Colpotomy, with exploration  
Dilation and curettage, diagnostic and/or therapeutic (nonobstetric)

#### **Group 4**

Laparoscopy

### Endocrine System

#### **Group 3**

Neurolisis (including carpal tunnel decompression)

#### **Group 4**

Ulnar nerve repair  
Ulnar nerve transfer

### Eye and Ocular Adnexa System

#### **Group 1**

Chalazion excision  
Discission lens (needling of lens)  
Foreign body removal  
Pterygium (excision or transposition)  
Lacrimal duct probing or reconstruction

#### **Group 2**

Canthoplasty  
Tarsorrhaphy

### **Group 3**

Ectropion/entropion repair

### **Group 4**

Cataract extraction  
Enucleation, with and without implant  
Iridectomy  
Eye muscle operation (extraocular muscles, strabismus procedure)

### Auditory System

#### **Group 1**

Myringotomy (including aspiration and/or eustachian tube inflation)

#### **Group 4**

Mastoidectomy, simple (transmastoid antrotomy)  
Myringoplasty  
Stapedectomy  
Tympanoplasty (without mastoidectomy)



## YEAR'S ADVANCES IN MEDICINE

The impact that technology has made on the art of medicine took a leap forward in 1982 as new methods of looking inside the human body and healing its ailing parts came out of the laboratory and into the hands of physicians.

Perhaps in no other single year have the strides in medicine received headline attention as often as they have this past year, said James H. Sammons, MD, executive vice president of the AMA.

Whether it has been the marvels of technology, as exemplified by the singular achievement of implanting the first permanent artificial heart, or the sincere efforts to improve the public health through prudent diet and exercise, Dr. Sammons said, the achievements in the healing arts continue to foster human dignity and well-being.

Among the events in medicine that will make 1982 so notable, the following would have to be mentioned:

**The artificial heart.** The historic surgery to implant the polyurethane plastic and aluminum Jarvik-7 heart into Barney Clark, DDS, came one day short of the 15th anniversary of the first human heart transplant.

**Nuclear magnetic resonance.** NMR and the machinery designed to apply it have the potential to revolutionize the way MDs look inside the body and their view of the body. NMR works with magnets instead of x-rays, eliminating the need for injected contrast dyes and radioactive solutions on which older, established diagnostic techniques depend.

The images are similar to those made by CT scanners in the sense that they are assembled with the aid of a computer and represent a cross-sectional view through an organ or an area of the body. NMR, however, can display a kind of biochemical blueprint of cellular activity as well as sharper and more detailed pictures than those produced by a CT scanner.

Investigators predict that NMR will detect certain diseases at earlier stages. Instead of showing physical alterations within the body, as conventional x-rays do (even when they are enhanced by a computer as CT scanner images are), NMR can show the actual chemical imbalance they may precede structural change.

**Medical lasers.** From their original use by ophthalmologists to weld detached retinas and seal leaking blood vessels in the eye, lasers continue to make inroads to areas of the body only the scalpel went before. Brain surgeons have used them to excise tumors; dermatologists focus the light-knife beams to eradicate skin cancer; and gynecologists have found lasers useful in some diseases of the female genital tract.

A new type of laser, pioneered in Europe and called the YAG laser (for neodymium yttrium aluminum garnet), is being used more and more for sealing bleeding ulcers.

On the forefront of laser technology is the laserscope, in which the light is transmitted through fiberoptics in a catheter. In experiments in the laboratory, a multichannel catheter—with a laser beamed through one channel—is being tested as a way to vaporize clotted material in the arteries that feed the heart.

**Streptokinase.** This clot-dissolving enzyme was approved by the Food and Drug Administration (FDA) this year for use in treating heart attacks. Given to appropriate patients in the early stages of a heart attack, the drug holds the potential for restoring circulation to a choked-off section of heart muscle and for preserving the vitality of the cells that otherwise would die.

**Cyclosporin.** Much of the credit for the improvement in survival after organ transplants—and the resurgence of transplant surgery—goes to this drug. Cyclosporin suppresses the production of cells called T-lymphocytes that are in the vanguard of the body's natural attack against foreign tissue—even when that tissue is beneficial, as it is in the case of transplants.

**Genetically engineered human insulin.** Human insulin made with recombinant DNA technology by genetically modified bacteria won FDA approval for marketing this year. Although it will not be available until 1983, the bioengineered insulin is the first such product made by gene splicing to be marketed for use in humans.

**Synthetic human interferon.** Genespinning techniques have led to the preparation of what promises to be an ample supply of interferon. In early clinical use, the synthetic variety has shown anti-cancer activity in patients with non-Hodgkin's lymphoma, breast cancer, chronic lymphocytic leukemia, Hodgkin's disease, and melanoma.

**Oncogenes.** A revival of a 10-year-old hypothesis with a startling cart-before-the-horse twist is producing some of the most promising research ever into the mechanism of cancer. The hypothesis and the related origin of the term oncogene (for cancer-causing gene) goes back to work done in the 1960s and early 1970s when certain viruses were found to have genes that cause cancer. The hypothesis held that infection of animal cells by such viruses leads to the incorporation of the so-called oncogene into the infected animal cell, which at some later date can become malignant.

This hypothesis took a surprising turn after research in recent years showed that oncogenes from viruses have identical counterparts in normal cells. It is now believed that the viral cancer gene—the oncogene—was captured from an animal cell sometime in the evolutionary past. In the current scenario, normal cells of animals and humans are thought to house oncogenes whose normal function is unknown. Under certain circumstances, it is hypothesized, these oncogenes could activate and lead to cancer.

**Hazards of salt.** A coalition of health organizations, federal agencies and food processors joined forces and found a voluntary way in which reliable information about the sodium content of packaged foods could be made available to physicians and to their patients whose daily sodium intake must be limited because of high blood pressure.

From American Medical News, January 7, 1983.





Rafael Villavicencio, MD

## ELECTROCARDIOGRAFIA PEDIÁTRICA

JCR es un niño de 8 años de edad con una cardiopatía congénita cianosante que cursa con hipovolemia pulmonar. A la edad de 1 mes se le hizo la primera anastomosis arterio-venosa para mejorar su hipoxia y su volemia pulmonar. Ha tenido un curso estable desde el punto de vista cardiovascular, excepto por una cianosis leve que se acentúa con el ejercicio, así como disnea al esfuerzo en ocasiones. Las derivaciones electrocardiográficas II (figura 1) y V<sub>1</sub> (figura 2) que se ilustran a continuación, se obtuvieron en una visita rutinaria de seguimiento.

Figura 1: Derivación II

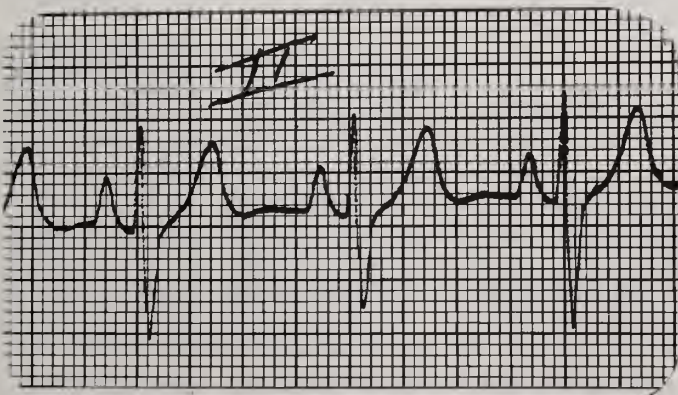
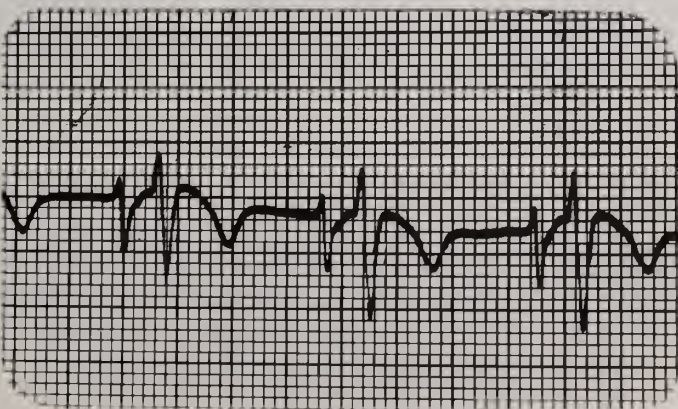


Figura 2: Derivación V<sub>1</sub>



## Sección de Autoevaluación

Estos trazados son compatibles con:

- a) bloqueo de rama derecha
- b) hipertrofia atrial derecha
- c) bloqueo A-V de 2º grado
- d) hipertrofia atrial izquierda
- e) hiperkalemia

Respuesta: b) Hipertrofia atrial derecha

### Análisis del Trazado

En ambas derivaciones se aprecia un ritmo sinusal regular con frecuencia atrial y ventricular de 75/min. El intervalo PR es de 0.16 sec. y el QRS de 0.10 sec. (límites superiores de normal). En la derivación II la onda P es positiva, de duración normal y picuda, con una amplitud de 4.5mm. En la derivación V<sub>1</sub> la onda P es bimodal (del tipo más-menos), con predominio de la negatividad. Su duración es también normal. Los hallazgos electrocardiográficos ilustrados son compatibles con una hipertrofia atrial derecha. El paciente tiene Atresia Tricuspídea tipo I-b.

### Discusión

Las características generales de morfología, amplitud, duración y polaridad de la onda P en niños en niños fueron discutidas en nuestro caso de Electrocardiografía Pediátrica anterior.<sup>1</sup> Por ello enfatizaremos la discusión en la peculiaridades de la onda P en la atresia tricuspídea (AT).

A pesar de que anatómicamente hay varios tipos de atresia tricuspídea, hemodinámicamente existen sólo dos: atresia tricuspídea con hipovolmeia pulmonar y atresia tricuspídea con hipervolemia pulmonar. En ellas algunos componentes del electrocardiograma (ECG) pueden variar, pero la onda P es similar para ambos casos: con hipovolemia y con hipervolemia pulmonar.<sup>2</sup>

El eje eléctrico de la onda P en AT es de dirección inferior y a la izquierda de +60 en el plano frontal. Las ondas P en las derivaciones I y II (sobre todo en esta última) usualmente exceden los límites normales de amplitud (2.5mm) y en muchas de ellas es de duración prolongada (figura 1). Aunque no es específica de AT, en algunos pacientes puede encontrarse una onda P bifásica en V<sub>1</sub>R y V<sub>1</sub> en la cual el terminal inicial positivo y el terminal negativo son picudos y de mayor amplitud (figura 2). Aunque la presencia de un terminal negativo y amplio sugiera hipertrofia atrial izquierda, estas ondas P se encuentran en pacientes con una dilatación marcada del atrio derecho, sin hipertrofia atrial izquierda.

En resumen, las propiedades importantes de la onda P en la AT son:

- a) onda P altas y picudas en las derivaciones I y II
- b) ondas P bifásicas en  $V_4R$  y  $V_1$  con terminales positivos y negativos profundos
- c) ondas P altas en las derivaciones precordiales  $V_2$  a  $V_6$ .

Ocasionalmente en AT hay una onda P amplia, con muesca, en la cual el componente inicial es mayor que el segundo; es la onda P *tricuspidale*.<sup>3</sup>

### Criterios de Hipertrofia Atrial Derecha

En pediatría estos son:

- ondas P altas ( $>2.5\text{mm}$ ) y picudas. Pueden apreciarse mejor en las derivaciones I y II.
- ondas P altas y picudas en los precordiales derechos, con un terminal negativo profundo.

### Situaciones Clínicas

El agrandamiento o hipertrofia atrial derecha lo podemos encontrar en las siguientes condiciones:

- 1) atresia tricuspídea
- 2) comunicación interatrial
- 3) retorno venoso anómalo total (supradiafragmático)
- 4) estenosis pulmonar severa
- 5) anomalía de Ebstein
- 6) tetralogía de Fallot severa
- 7) cor pulmonale
- 8) hipertensión pulmonar primaria

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### BLOOD LIPID THERAPIES ENDORSED

Recommendations regarding the efficacy of dietary and pharmacologic therapy in altering blood lipid concentrations have been approved by the American medical Association House of Delegates.

The recommendations, made by an advisory panel of expert consultants convened by the AMA Council on Scientific Affairs, address the treatment of the individual patient who, because of hyperlipidemia, is at significant risk of coronary heart disease.

The recommendations are that:

- Initial search for the presence of hyperlipidemia ideally be done at or before age 20.

- Prior to initiating treatment, fasting levels of plasma cholesterol and triglyceride should be measured at least twice, to determine a base-line value. Lipoprotein studies are not ordinarily necessary before initiation of therapy.

- Underlying disorders such as alcoholism, diabetes, or hypothyroidism, known to cause elevation of plasma lipoproteins, should be identified and treated directly when present.

- Vigorous dietary therapy should be initiated in patients who have mean serum cholesterol levels above the 90th percentile for age and sex. Patients under 60 who continue to have plasma lipid elevations unresponsive to dietary therapy deserve a trial of long-term drug therapy.

- Patients with plasma lipid levels in the range of the 50th to 90th percentile for age and sex also may benefit from diet therapy, because the majority of coronary heart disease patient emerge from this group. Factors such as age, sex, family history, accompanying disease, prognosis, and anticipated compliance all may influence the clinical decision to treat the hyperlipidemia.

- Diet therapy of hypercholesterolemia and hypertriglyceridemia should include instruction in attaining and maintaining a desirable body weight. Further measures include a diet that contains no more than 30% to 35% of calories as fat, less than 10% of calories from sources of saturated fat, and at least 10% of calories from oils rich in polyunsaturated fatty acids. These should be less than 300 mg/day of cholesterol with an adequate protein intake.

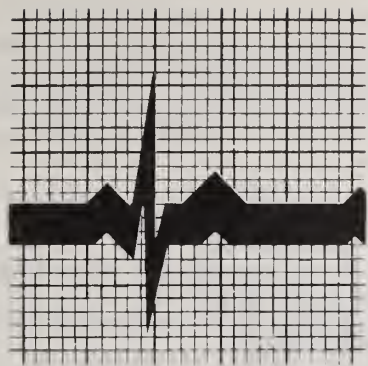
- In patients who have not reached an optimal level of plasma cholesterol on the above diet, further restriction of fat to less than 30% of calories and cholesterol to less than 250 mg/day may be warranted.

- If the plasma triglyceride level remains above the 90th percentile, alcohol should be proscribed and carbohydrate restriction may be necessary. Drug therapy usually is not justified in isolated hypertriglyceridemia.

- Because of the fact that one family member with hyperlipidemia suggests that other members may be at risk, and because dietary management is a family affair, consideration should be given to extending the dietary recommendations to the patient's entire family.

- Control of plasma lipid levels is only one facet in cardiovascular risk management. Other factors such as stopping cigaret smoking, blood pressure control, and the medical management of glucose intolerance must not be ignored.





# ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD, FACC  
Osvaldo Jiménez, MD

This was a 61-year-old male with a history of diabetes mellitus, alcoholism, hypertension and an old myocardial infarction (MI) in 1966. During the last month he had been hospitalized elsewhere because of acute pulmonary edema and renal insufficiency. He was transferred to the University Hospital for dialysis. Laboratory data were: Hb 4.7 g, BUN 118 mg/dl, serum potassium 4.6 meq/L; the chest roentgenogram showed biventricular enlargement and congestive heart failure. Therapy consisted of digoxin, diuretic and lidocaine. Electrocardiograms (ECG) of 11-6-81 to 11-9-81, are illustrated in Figures 1-3.

Figure 1

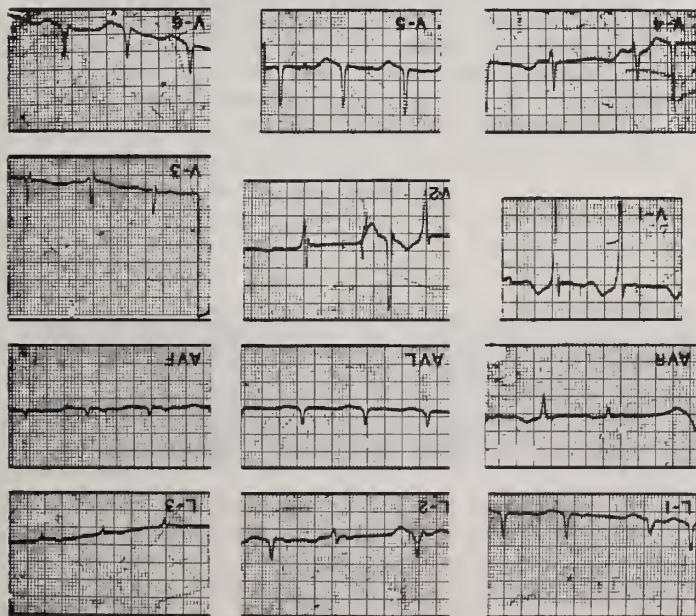


Figure 2

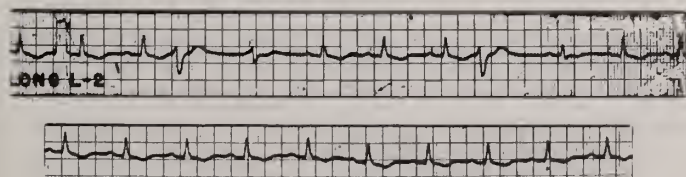
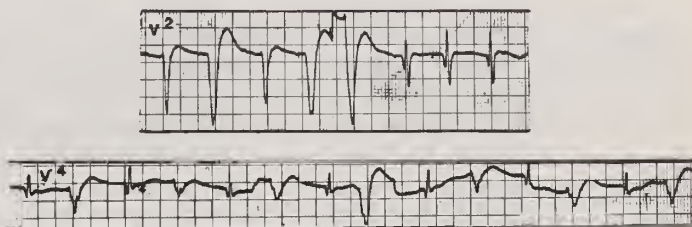


Figure 3



## Questions

1. What are the electrocardiographic diagnoses?
2. What is the underlying electrophysiology of the arrhythmia?

## Answers

Autopsy revealed pericardial fluid, 3-vessel coronary artery disease and infarction of the cardiac apex, septum and two-thirds of the anterior wall.

The complete ECG in Figure 1 demonstrates normal sinus rhythm (NSR), left ventricular hypertrophy with strain, multifocal premature ventricular beats (PVB)—some as infarction PVBs— anterior and possibly inferior MIs. The post premature beat pauses are terminated by beats in leads 11 (rS), aVR, V<sub>2</sub> and possibly V<sub>4</sub> with a left anterior hemiblock (LAH) type of intraventricular conduction. Those in leads 11, aVR and V<sub>4</sub> may be sinus conducted beats with LAH conduction, suggesting phase 4 LAH. The P-R intervals are approximately 0.15 S. The third beat in V<sub>2</sub>, as a slightly accelerated junctional escape beat (AJEB) of Q/RS configuration, unmasks the anterior MI which is not evident in the first beat. The third beat in V<sub>4</sub> appears to be conducted with aberration but yet is similar to the second premature beat.

Figure 2 strips show NSR and two PVBs. The pause after the first PVB is terminated by an AJEB with LAH conduction. The pause after the second PVB is fully compensatory, the subsequent beat being a sinus conducted beat (P-R interval 0.18 S) with aberration (or a ventricular fusion beat - sinus beat plus junctional beat). Both the escape beat and the sinus beat appear to be conducted with phase 4 LAH.

In Figure 3, lead V<sub>2</sub>, the second, fourth and fifth beats are end-diastolic PVBs. The last of these is followed by an

accelerated junctional escape rhythm (P-R distance 0.12 S in the first beat, questionably conducted), unmasking the anterior MI, which suggests phase 3 LAH. In  $V_4$  the basic QRS complexes are similar to those in  $V_3$  of Figure 1. Multifocal ventricular bigeminy is present, and appears to produce simple retrograde concealed conduction, as the P-R interval is longer, approximately 0.20 S. The PVBs in lead  $V_2$  (QR) and  $V_4$  of Figure 1 and the two PVBs of Figure 2 (rS) have similar coupling and could be of fascicular origin, arising near the posterior-inferior fascicle of the left ventricle.

Both relatively early and relatively late junctional escape beats unmask the anterior MI. Thus, this may be a function of the LAH, rather than being cycle length dependent alone.

### Discussion

Ventricular escape beats may be near normal or may be conducted by minor degrees of incomplete right or left bundle branch block or hemiblock.<sup>1</sup> Aberration of junctional escape beats and bradycardia-dependent blocks has been attributed to various causes: 1) a lack of the complex cancellation and channeling that usually accompany the transmission of sinus impulses through the atrioventricular (AV) node, 2) desynchronization of the normal sequence of depolarization in the AV junctional area, and asynchronous spread down the His Bundle and bundle branches, 3) conduction of AV nodal impulses to the ventricles through ectopic preferential pathways such as paraspecific fibers of Mahaim, 4) supernormality of intraventricular conduction, 5) Wenckebach facilitation/phenomenon, 6) a functional transverse or longitudinal dissociation within a main bundle branch, 7) vagotonia, 8) concealed conduction, hypoxia, stretching of the conducting tissues resulting from overfilling during the long diastolic intervals, 9) and abnormal site of origin such as an escape beat arising in the posterior-inferior fascicle of the left bundle branch may produce a complex of minor incomplete right bundle branch block and LAH, 10) hypopolarization secondary to enhanced phase 4 depolarization of latent pacemaker cells in the bundle branch system.<sup>1-4</sup>

Schamroth<sup>1</sup> defines "Bradycardia-dependent Hemiblock" as relatively late beats being associated with hemiblock conduction whereas slightly earlier beats have normal intraventricular conduction.

Elizari et al<sup>5</sup> described the first case of this as bradycardia-dependent and tachycardia-dependent LAH in the same patient. The bradycardia-dependent hemiblock appeared with progressive lengthening of the R - R intervals which resulted in progressively increasing degrees of LAH.

Girotti<sup>6</sup> et al have described phase 4, bradycardia-dependent left posterior hemiblock.

LAH is known to mimic anteroseptal MI.<sup>7-8</sup> Phase 3 and phase 4 LAH beats presenting as sinus conducted beats and AJEBs in this patient unmasked an anterior MI.<sup>9-11</sup> Premature ventricular or supraventricular beats may reveal MI as shown in this patient.<sup>7-12</sup> Additionally, evidence of MI was present in the junctional escape beats. Rate dependent right precordial Q waves may reflect a "septal focal block" without or with a MI.<sup>12</sup>

Both premature and escape AV junctional beats may present with an altered QRS morphology (ventricular activation), believed due to fusion between a sinus beat and an AV junctional beat conducted via an unusual pathway to the

ventricles.<sup>3</sup> Also, in this context a ventricular escape beat must be differentiated.<sup>4</sup> The QRS pattern is similar for phase 3 and phase 4 LAH. The phase 4 LAH in this case is revealed during the long pause following a PVB, similar to paroxysmal AV block subsequent to atrial or ventricular extrasystoles.<sup>13</sup>

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# Resúmenes de La Literatura Médica

## **PREVENTION OF GROUP B STREPTOCOCCAL COLONIZATION WITH TOPICALLY APPLIED LIPOTEICHOIC ACID IN MATERNAL-NEWBORN MOUSE MODEL. F. Cox, *Pediatr Res* 16: 816-819, 1982**

La infección por los estreptococos del grupo B es una importante causa de morbilidad neonatal. La forma temprana se caracteriza por sepsis y meningitis y se adquiere en el tracto ano-genital materno. Se ha intentado la prevención mediante el tratamiento de la madre o el neonato con antimicrobianos y los resultados han sido variables. "Lipoteichoic acid" (L.A.) proviene de la pared celular del estreptococo y tiene la función de ligar este a la mucosa. L.A. purificado aplicado en forma tópica antes de inducir la infección con estreptococos del grupo B evita la colonización por estos en ratones de un día de edad. Esta es la primera vez que se demuestra en vivo la prevención de este tipo de infección mediante la interferencia con la adhesión del microorganismo.

José E. Sifontes, MD

## **CIERRE ESPONTANEO DEL DEFECTO INTERATRIAL FOR FORMACION DE ANEURISMA INTERATRIAL: Awan IH, Rice R, Moodie DS, *Ped. Cardiol* 1982, 3(2):143.**

El Departamento de Cardiología del Cleveland Clinic Foundation informa del caso de una niña con un defecto interatrial documentado por medios invasivos a la edad de 7 meses el cual cerró espontáneamente mediante la formación de un aneurisma del septo interatrial. El cierre del septo fue comprobado a la edad de 6 años mediante estudios no-invasivos como: ecocardiografía bidimensional con contraste; estudios de radionucleidos y angiograma por substracción digital.

Hay pocos casos de cierre espontáneo del defecto interatrial en la literatura médica occidental. Los mecanismos aceptados para este cierre son: por la formación de trombos; mediante proliferación fibrosa; y ahora por formación de un aneurisma septal. Estos mecanismos son los que se describen también en el cierre espontáneo de los defectos del septo interventricular.

La importancia de este artículo es dual, ya que por un lado se describe por primera vez este mecanismo de cierre del septo interatrial; a la vez que se demuestra como con el uso adecuado de pruebas diagnósticas no-invasivas este hallazgo de tanto valor pronóstico ha logrado confirmarse.

Rafael Villavicencio, MD

## **CLINICAL COURSE OF ESOPHAGEAL STRICTURE MANAGED BY BOUGIENAGE. ME Glick. *Digestive Disease & Sciences* 27: 884, 1982.**

El autor evaluó la frecuencia de recurrencia de disfagia en pacientes que se les dilató el esófago con dilatadores del tipo de Maloney. Todos los pacientes tenían estrechez del esófago por enfermedad péptica y se excluyeron del análisis los pacientes que tenían escleroderma, Raynaud's o cirugía gástrica previa. Cuarenta y seis de 71 pacientes (65%) tuvieron recurrencia de disfagia y necesitaron dilatación nuevamente. De los que necesitaron dilatarse una segunda vez, la probabilidad de necesitar dilataciones adicionales era entre 0.86 a 0.95. El promedio de tiempo entre la primera dilatación y la recurrencia de disfagia fue de 8 semanas. Mientras más dilataciones se requerían en un paciente el intervalo entre una dilatación y la siguiente se aproximaba a 4 semanas. En la duración del estudio se hicieron 56 dilataciones, y hubo una perforación de esófago pero no hubo muerte asociada con bougienage.

Angel Olazábal, MD

## **PERTURBATION OF GASTRIC EMPTYING AND DUODENAL MOTILITY THROUGH THE CENTRAL NERVOUS SYSTEM. D.G. Thompson, E. Richelson, and S.R. Malagalada. *Gastroenterology* 83: 1200-1206, 1982.**

No hay muchos datos sobre la influencia del sistema nervioso central (SNC) en las funciones del aparato gastrointestinal. En este estudio los autores evaluaron si los estímulos que actúan sobre el SNC perturban la respuesta usual gastrointestinal a una comida. Evaluaron la motilidad gastrointestinal,

vaciamiento del estómago y secreción de ácido gástrico en 4 voluntarios normales en respuesta a vertigo inducido por irrigación del oído con agua a 4°C. Se encontró que la estimulación del laberinto causa un retraso marcado del vaciamiento de la comida del estómago al duodeno. Este estudio demuestra que estímulos que actúan en el SNC pueden alterar la función gastrointestinal en personas normales.

Angel Olazábal, MD

**CHANGES IN INDICATIONS FOR HEART TRANSPLANTATION: AN ADDITIONAL ARGUMENT FOR THE PRESERVATION OF THE RECIPIENT'S OWN HEART.** Losman, J.G., Levine, H., Campbell, C.D., et al. *J. Thorac Cardiovasc. Surg.* 89: 716, Nov. 1982.

Los autores revisan la experiencia con trasplantes heterotópicos en el Hospital Groote Schuur en Sur Africa, donde por primera vez se llevó a cabo un trasplante cardíaco humano en 1967. Comentan sobre la mejoría en la sobrevida a un año después de trasplantes cardíacos, que ha aumentado desde 30% a 70%; y la sobrevida a 5 años que es de 50% actualmente. Los autores consideran que el trasplante heterotópico, donde se injerta el corazón donante como auxiliar al corazón recipiente, tiene ciertas ventajas sobre el clásico trasplante ortotópico donde se remueve el corazón del recipiente en su totalidad. En 40 pacientes que fueron sometidos a estos trasplantes heterotópicos, la sobrevida fue de 73% a seis meses, 65% a doce meses, 51% a los 36 meses. Por diferencias en criterios de selección y debido al progreso que se ha demostrado en la inmunología de trasplantes, esta mejoría en sobrevida no se puede adjudicar directamente a ventajas de los trasplantes heterotópicos, pero sugiere ciertas ventajas teóricas.

Pedro J. Rosselló, M.D., F.A.C.S.

**RESULTS OF COMBINED BILIARY DRAINAGE AND CHOLECYSTOKININ CHOLECYSTOGRAPHY IN 81 PATIENTS WITH NORMAL ORAL CHOLECYSTOGRAMS.** Burnstein, M.J., Vassal K.P., Strassberg, S.M. *Annals of Surgery* 196: 627, Dec. 1982.

El paciente ocasional que presenta síntomas y cuadro clínico típico de colelitiasis pero cuya patología no se puede confirmar por métodos diagnósticos usuales, constituye un reto al clínico. Los autores evaluaron 81 pacientes con sospecha de patología de las vías biliares pero con pruebas negativas de colecistograma oral y de ultrasonido abdominal. Utilizando una prueba conjunta de aspiración de bilis duodenal (BD) y de radiografía con infusión de colecistokinina (CC), encontraron 35% con resultados positivos, 14% con resultados sospechosos y 51% con resultados negativos. Hubo una correlación alta entre el grupo que demostró resultados positivos, y hallazgos positivos al hacer una colecistectomía y la mejoría sintomática de estos. En aquellos que las pruebas resultaron negativas y se operaron, se identificaron menos hallazgos patológicos y el resultado sintomático fue menos dramático.

Se recomienda este método para el caso problemático de síntoma característicos de patología de vías biliares sin confirmación por otras pruebas diagnósticas.

Pedro J. Rosselló, M.D., F.A.C.S.

**TRATAMIENTO DE MIELOMA MULTIPLE E INFECCION TEMPRANA:** Perri et al. *Am J Med* 1981, 71:935.

El tratamiento de mieloma múltiple ha sido asociado con un aumento en la frecuencia de pulmonías pneumocócicas. Estudios recientes indican que también ocurre un aumento en la frecuencia de infecciones por organismos gram-negativos. Perri y colaboradores hicieron un estudio con 62 pacientes con mieloma múltiple que habían sido tratados con terapia inductiva con melphalan, predisona o BCNU, ciclofosfamida, y/o combinaciones de predisona. Observaron 143 infecciones con una incidencia de 1.46 infecciones por paciente/año y 4.68 infecciones por paciente/año en los primeros dos meses de quimioterapia. Avanzado en el tratamiento, el riesgo de infección disminuyó a 1.04 infecciones por paciente/año e incluyó pacientes que se habían recuperado de infecciones iniciales, indicando que este sub-grupo no tenía mayor riesgo de recurrencia.

Las infecciones que ocurrieron temprano en el tratamiento con quimioterapia fueron causadas, en 15 casos por bacterias gram-positivas, y en 24 casos por bacterias gram-negativas; hubo infecciones mixtas en 2 casos. Al preparar cultivos, los organismos predominantes resultaron ser *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* y *Pseudomonas aeruginosa*. Predominaron las infecciones respiratorias (48%) y el tracto urinario (36%). Se encontraron hemocultivos positivos (blood isolates) en aproximadamente 25%. Hubo una tasa de mortalidad de un 17% en estas infecciones tempranas; hubo una tasa de mortalidad alta en pacientes con sepsis gram-negativa. La mortalidad se asoció también con niveles de creatinina de 2 mg/dl o más altos y con pacientes de 65 años o mayores.

**Comentarios:** El mieloma múltiple se ha asociado con malfuncionamiento de anticuerpos que contribuye a infecciones tempranas con *S. pneumoniae*. La predisona y los agentes citotóxicos suprimen los elementos de la médula ósea agravando así las anomalías inmunológicas y aumentando el riesgo de infección. Los primeros dos meses de terapia son críticos; ésto es así debido a las dosis altas de quimioterapia y a que se utilizan otras modalidades terapéuticas en casos con complicaciones como hipercalcemia. Estamos de acuerdo con los autores en que los antibióticos profilácticos y la inmunoterapia en esta fase temprana de tratamiento para mieloma múltiple pueden ser útiles en la protección de los pacientes, pero, hasta el momento, no hay disponible un régimen definitivo o bien estudiado.

C.H. Ramírez-Ronda, M.D.



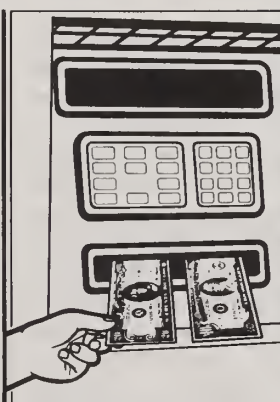
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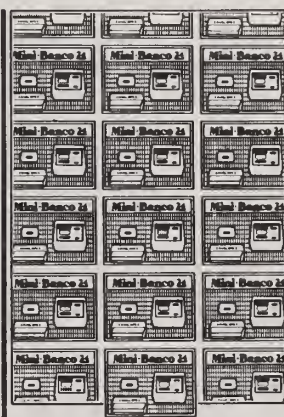
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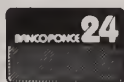
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# Medicolegal Decisions



## STIPENDS PAID TO RESIDENTS NOT TAXABLE COMPENSATION, FEDERAL APPELLATE COURT RULES

Stipends paid to physicians when they were residents at a University Medical Center were scholarships or fellowships and not taxable compensation, a federal appellate court for Missouri ruled.

The physicians served in residency programs in the departments of medicine, anesthesiology, or dermatology at the University Medical Center to attain the necessary training and prerequisites for board certification in the various areas of specialization. The residents excluded portions of stipend payments from the university from their federal income tax computations of gross income for the taxable years 1972, 1973, and 1974.

The Internal Revenue Service then asserted that the excluded stipend payments were not excludable scholarships or fellowships and assessed additional taxes, which the physicians paid. Upon subsequent denial by the IRS of their claims for refunds, the physicians filed separate suits seeking refunds. The suits were then consolidated for trial, and the jury found that the stipends were scholarships or fellowships and not taxable compensation.

On appeal by the U.S., the federal appellate court affirmed the decision for the physicians. However, the court ruled that the form of verdict used by the trial court was erroneous because the jury's role was not to determine whether the stipend was to be excluded under the Internal Revenue Code. The jury, acting as a fact-finder, was to determine only the factual issue, to wit, whether the primary purpose for which the payments were made was for services rendered or whether the payments were fellowship or scholarship grants, as legally defined by the court.

Nevertheless, the court said that it would not reverse the jury's determination of a factual question where the verdict was supported by substantial evidence; nor would it as an appellate court substitute its judgment for that of the jury or judge sitting as fact-finder.

The appellate court disagreed with the U.S.'s argument that, in light of the overwhelming number of factually similar cases which have held against taxpayers on this exclusion issue, reasonable minds could not hold to the contrary in this case. "Although significant evidence to support the Govern-

ment's argument that the stipends were in the nature of compensation, or were *quid* for the *quo* of services, admittedly exists, the jury's verdict must be upheld unless reasonable minds, viewing the evidence in the light most favorable to the prevailing party, could *only* have found *otherwise* than fact-finder," the court said.

After reviewing the duties of hospital residents and the objectives of the residency program, the court concluded that there was substantial evidence that the residents' stipends were in the nature of scholarships or fellowships.—*Mizell v. U.S.*, 663 F. 2d 772 (C.A.8, Mo., Oct. 29, 1981)

## PARENTS, BUT NOT CHILD, CAN RECOVER DAMAGES FOR CHILD'S BIRTH DEFECT

The parents of a deformed child had a cause of action against four physicians for failure to diagnose or warn of an inheritable disease, a Florida appellate court ruled.

The mother suffered from Larsen's Syndrome, which caused her physical problems, mental suffering and substantial expenses for medical care since birth. She and her husband decided to have a child and sought medical advice from the obstetricians and gynecologists as to whether the condition was inheritable. The physicians failed to advise the parents that the condition was inheritable. A child was conceived and born with Larsen's Syndrome.

In an action against the physicians, the parents sought to recover for past and future medical expenses for the extraordinary care in treating the child; past and future emotional pain and suffering resulting from the birth; physical pain and suffering from her pregnancy; and costs of bringing the action. The child sought damages for wrongful life. A trial court dismissed the claims, and the parents and child appealed.

Stating that the child had no cause of action for wrongful life, the appellate court affirmed dismissal of that claim. However, the parents had a cause of action against the physician for their failure to diagnose and inform them that the mother's condition was inheritable. They could recover medical expenses and the cost of extraordinary care for treatment of the child's physical abnormalities in excess of the cost of rearing a normal child, the court said. They could not recover damages that arose from the mother's pregnancy and for past and future emotional pain and suffering from the birth of the child because her pregnancy and delivery were no more difficult and painful than if the child had been normal, the court said. Further, they could not recover the cost of bringing the action, the court concluded.—*Moore v. Lucas*, 405 So.2d 1022 (Fla. Dist. Ct. of App., Oct. 28, 1981; rehearing denied, Nov 23, 1981)



## ER. PHYSICIAN AND HOSPITAL SUED FOR ALLEGED NEGLIGENCE

Summary judgment was inappropriate in malpractice actions against a hospital and two physicians, a federal trial court in Georgia ruled.

A patient died at home on August 15, 1978. Two days earlier he had gone to the hospital's emergency room complaining of chest pains, shortness of breath, tooth pain, and other ailments. he was examined by the physician on duty in the ER. The physician allegedly misdiagnosed the patient's ailment and failed to order tests that would have revealed the actual cause of the symptoms. The ER physician was a member of a group of physicians who provide emergency room services to the hospital.

In 1975, three physicians signed a contract with the hospital to provide emergency room services. Each signed individually, not on behalf of the group. The physicians charged a standard fee to ER patients and the hospital billed the patients and paid the group 80 per cent of its collections. The hospital guaranteed \$16,666.66 per month and the physicians divided the money in proportion to the hours each worked. At the time of the alleged malpractice, one of the initial members had left. The physician who saw the patient in the ER had been recruited to provide full-time service to the ER. The contract was never amended, and he never signed it. He was paid an hourly rate and did not participate in any overage or excess payments to the group. His hourly rate was somewhat less than that paid to the other physicians in the group. He paid his own taxes and malpractice insurance premiums.

The patient's estate named the ER physician, the physician who was head of the group, and the hospital as defendants. on motions for summary judgment by the hospital and the head of the group, the trial court said that summary judgment was improper because of questions concerning the relationship among the physicians and the hospital. A jury should decide whether the head physician could be held liable for the negligence of the treating physician on the theory that the treating physician was his employee. The court reviewed earlier cases discussing the employee-independent contractor controversy and set out the factors Georgia courts had considered in those decisions.

The court said it would be consistent with the principle that an employer is liable for the negligence of his employees if the head physician were held liable. He and the group profited from the treating physician's services because the treating physician was paid less than other group members, the court said. Because there were conflicting decisions in prior cases, a jury should decide the liability of the head physician, the court said.

The hospital's liability should also be decided by a jury. The hospital may be estopped from denying liability for the treating physician's acts on the doctrine of apparent authority. If the estate can show that the patient relied on the hospital and its apparent agent to provide treatment, the hospital could also be liable for the treating physician's acts, just as if he were an employee, the court concluded.—*Stewart v. Midani*, 525 F. Supp. 843 (D.C., Ga., Nov. 5, 1981)

## NO NEGLIGENCE BY MD IN PERFORMANCE OF SURGERY

A physician and a hospital were not negligent in performing an operation on a patient to correct an anal fistula and hemorrhoids, a Louisiana appellate court ruled.

The physician diagnosed the patient's rectal problems as an anal fistula and hemorrhoids. He recommended surgery to cut out the inflamed tissue and remove the hemorrhoids. She consented to the operation, and it was performed on November 3, 1969. The physician removed the hemorrhoids, a fissure, a fistula and associated scar tissue located in the anal canal and in the external sphincter. The drainage and infection from the fistula had caused inflammation, infection and scar tissue in the external sphincter muscle. The physician cut a substantial part of the scar tissue from the sphincter.

After the operation, the patient complained of continued pain and fecal incontinence. She contended that her problems were caused by the physician's negligence in performing surgery. A trial court ruled in favor of the physician and the hospital, and the patient appealed.

Affirming the decision, the appellate court said that *res ipsa loquitur* did not apply to her claim. The patient stated that she had pain in her rectum and in her back, right hip and right leg. That pain was not consistent with her theory that the surgeon's negligence was the most plausible explanation for her injury. Four physicians testified at trial that an explanation for the pain could be the formation of a neuroma in some scar tissue resulting from surgery. Another possible explanation for the pain could be the formation of a neuroma in some scar tissue resulting from surgery. Another possible explanation was a diseased disc in her back, a condition that had been diagnosed by an orthopedic surgeon, the court said.

Even if the physician had failed to inform the patient that she could have pain after surgery because cut nerves might become imbedded in scar tissue and that she might have some incontinence because of necessary surgical damage to the external sphincter, the failure did not void the patient's consent. One of the risks of not having surgery was that the fistula could cause septicemia or cancer if it were not removed. The court said that a prudent person would have consented to surgery because of the risk of not having it.—*Zeno v. Lincoln General Hospital*, 404 So. 2d 1337 (La.Ct. of App., Sept. 29, 1981).

## MOTHER CLAIM SHE GOT POLIO AFTER SON'S SHOT

A victim of polio had a claim against the government for negligence in not following its own regulations in licensing a live oral polio-virus vaccine, a federal appellate court for Arkansas ruled.

The patient contracted polio after her infant son was inoculated with a trivalent, live, oral polio vaccine. She was stricken with a vaccine-associated case of polio-myelitis, Type

2, within a month after her son's inoculation. As a result, she became a paraplegic. She filed suit under the Federal Tort Claims Act based on the government's negligence in licensing the vaccine without requiring the manufacturer to produce information required by regulation; in licensing the Sabin vaccine without establishing that it was safe for persons in close proximity to those who were inoculated; and failing to use due care in approving the specific lot used to inoculate the patient's son. A trial court dismissed the complaint, and the patient appealed.

On appeal, the appellate court said that the government was immune from suit for failure to issue regulations governing the effect of shed virus from the vaccine on third persons. Whether to issue a regulation was a discretionary government function, which was immune from suit, the court said. As to the claim that the government failed to follow its own regulations in licensing the vaccine or releasing the particular lot for distribution, the court said, that the patient stated a cause of action on that claim. The government had no discretion to disregard the mandatory regulations on licensing and releasing the vaccine, the court said.

The trial court's dismissal was affirmed in part and reversed in part.—*Loge v. U.S.*, 662 F. 2d 1268 (C.A.8, Ark., Nov. 6, 1981).

#### MD CANNOT SUE PATIENT'S ATTORNEYS FOR NEGLIGENCE

A physician cannot sue a patient's attorneys for negligence, a Michigan appellate court ruled.

The law firm had filed a medical malpractice action, seeking damages for the physician's failure to diagnose an ectopic pregnancy from X-rays. His review of a hysterosalpingogram on June 28, 1972, detected no ectopic pregnancy. On July 2, the patient required surgery for a ruptured fallopian tube. Three years after the malpractice action was filed, it was formally discontinued.

The physician then filed a countersuit against the attorneys who had represented the patient in the malpractice action. He alleged that the attorneys were negligent in failing to investigate the merits of the patient's claim prior to commencing suit. The complaint alleged negligence and malicious prosecution. A trial court dismissed the negligence count, but denied the attorneys' motion for summary judgment as to the claim of malicious prosecution.

On appeal by the physician the appellate court affirmed the trial court's grant of summary judgment on the negligence count. The appellate court relied on other cases denying recovery. The attorneys for a patient in a medical malpractice action did not owe a legal duty to the physician to investigate their client's claims of malpractice prior to suit, the court said. Strong public policy encouraging free access to the courts and prior case law dictated a finding of no cause of action for negligence against the attorney by the physician, the court concluded.—*Schunk v. Zeff & Zeff, P.C.*, 311 N.W. 2d 322 (Mich. Ct. of App., Sept. 9, 1981).

#### PHYSICIAN LIABLE FOR INJURIES FROM UNLAWFUL SILICONE INJECTIONS IN BREASTS

An award of \$450,000 in special and general damages and \$1,500,000 in punitive damages against a physician who

unlawfully injected silicone into a woman's breasts was not excessive, a California appellate court ruled.

In May 1968, the patient consulted the physician with regard to breast augmentation. The physician said that implants were not satisfactory but that he had a simple, inexpensive procedure, free of side-effects, that could be done in his office. The patient agreed to injections of an "inert substance". About a month later, when she went for a second set of injections, she overheard the physician mention the word silicone.

In November 1968, the patient consulted another physician because of lumps in her breast. She told him she had received silicone injections. The physician found additional lumps and referred the patient to surgeons for further evaluation. The physicians decided to monitor the patient closely but not perform a biopsy at that time.

In July 1971, the physician operated and found that a mass in each breast had overtaken the normal breast tissue and that there were enlarged lymph nodes under both arms. A double mastectomy was performed, and masses were also removed from the patient's waist and shoulders. No malignancy was found.

Additional silicone was removed two years later. During this time, the patient suffered emotional distress reactions, with fear of cancer, and sought psychiatric help for depression and was unable to care for her children and house. Her husband left her several times, and they ultimately divorced.

In November 1971, the patient filed a complaint against the physician who performed the implantations, alleging malpractice and assault and battery by use of an illegal substance. Fraud and intentional infliction of emotional distress were later added to the complaint. The court granted summary judgment for the physician on the cause of action for malpractice, based on the one-year statute of limitations. The court ruled that application of the statute of limitations for fraud and for assault and battery was a jury question. The jury decided in favor of the patient.

On appeal, the physician contended that all of the patient's causes of action were for injuries resulting from medical treatment and were controlled by the one-year statute of limitations for malpractice. He also complained of admission of evidence pertaining to his arrest in February 1968, for use of silicone, which was considered dangerous for use in the human body without a permit.

The court found that the evidence was admissible to rebut the physician's statements including the statement that he had first become aware in 1970 that a permit was required for injection of silicone. The court also upheld admission of testimony by a former employee of the physician that he told her in 1967 that silicone injections were unlawful and that he gave such injections to a number of women in 1967 and 1968.

The court said that the physician injected silicone into the patient without telling her its name or that it could be used only under scientific circumstances and with a permit. The court found that there was evidence that the procedure to which the patient consented was sufficiently different from that which was performed to amount to a battery. Where the physician knowingly represented that he could safely administer the substance and administered it without the required permit, the patient could maintain an action for fraud, the court said. Nor did the trial court abuse its discretion by allowing the patient to amend her complaint to include an action for intentional infliction of emotional distress. The court found that the trial court properly concluded that the



longer limitations period was applicable and that the jury should decide each cause of action.

The appellate court affirmed the trial court's decision.—*Nelson v. Gaunt*, 178 Cal. Rptr. 167 (Cal. Ct. of App., Nov. 13, 1981).

### COURT TO PERIODICALLY REVIEW ALIMONY PHYSICIAN MUST PAY TO HIS EX-WIFE

A divorce decree providing a trial court would periodically review the alimony a physician had to pay his ex-wife should be affirmed, an Ohio appellate court ruled.

The parties had been married in 1969. She was a teacher and he was a pharmacist. In the fall of 1971, he began attending medical school in Guadalajara, Mexico. After his graduation in 1975, he completed a mandatory program for foreign-educated medical students. He completed his internship and began a two-year residency in June 1977.

The physician filed for divorce in May 1977, stating grounds of gross neglect of duty. A trial court awarded the physician's wife a divorce and custody of their son. The court ordered the physician to pay her \$250 per month alimony until further order, \$150 per week as child support, \$7,500 for attorney's fees, \$1,029.80 for costs advanced \$1,200 to reimburse her parents for child support they furnished after the separation, and to pay the marital debts of \$17,900.

On appeal, the wife contended that the court erred in failing to find that the physician's medical license was marital property subject to division. She said that its present value was \$863,702 as calculated by an expert using statistics. The appellate court said that the physician's license was an asset but it was not subject to precise division. It was one factor to be considered in the award of alimony, the court said. The trial court's order was not erroneous in view of the facts that the wife was qualified to work as a teacher full-time and that her hours were particularly appropriate for rearing a minor child, the physician had substantial financial obligations facing him in the immediate future, and he was not yet earning a substantial salary.

The provision for periodic review of the amount of alimony was appropriate, the court said. The lower court's decision was affirmed.—*Lira v. Lira*, 428 N.E.2d 445 (Ohio Ct. of App., April 17, 1980).

### U.S. NOT LIABLE FOR MURDER BY VA PSYCHIATRIC PATIENT

The U.S. government was not liable for the death of a man who was murdered by a psychiatric out-patient of the Veterans Administration, a federal trial court in Ohio ruled.

The patient had been seen sporadically as an outpatient at a VA mental health clinic between January 1966 and December 1975. He was diagnosed as schizophrenic. At his last psychiatric examination, in May 1975, the diagnosis indicated that he was competent, perhaps under the control of his medication.

In February 1977, the patient committed murder. He was convicted and sentenced to prison. The executrix of the murder

party's estate sued the government under the Federal Tort Claims Act, claiming that the government was liable for the death.

At the trial, experts testifying for the executrix and for the government agreed that outpatient treatment and medication of the patient were appropriate and in accordance with medical standards.

When last seen at the clinic, the patient was functioning satisfactorily in the community, was competent, and was capable of holding a job. There was no indication that he was a danger to himself or anyone else.

The court said that the executrix had the burden of proof in establishing the knowledge or likelihood that the patient would cause harm to others. The court found that she had failed to sustain that burden of proof. Holding that the government had no liability for the patient's actions 14 months after his last date of treatment where community standards were followed, the court dismissed the suit.—*Case v. U.S.*, 523 F. Supp. 317 (D.C., Ohio, Sept. 25, 1981).

### A \$12,400,000.00 VERDICT?

A startling reminder of how far things have proceeded in a wrong direction was issued this week by a jury in Florida which handed down a \$12.4 million damage verdict in favor of a young woman, victim of failure of an oxygen dispensing machine to function properly while she was on the operating table.

Such a verdict is compassion carried to an extreme, considering that the real beneficiary is not the young woman, who is in a coma and in no position to enjoy it, but her lawyer, who gets a \$4.9 million fee...

The legislatures need to make sure that patients who put themselves in the hands of doctors and hospitals shoulder a fair share of the responsibility for what happens to them...

Perhaps that leaves the door open for some doctors to make mistakes and get away with it. It accepts something less than perfection. To insist on perfection in medical treatment is unrealistic, though. To attend lack of perfection with massive damage awards that frighten doctors away from their jobs, send the cost of medicine soaring and make lawyers fat at everybody else's expense is crazy.

Arthur M. Wilcox, *The News and Courier*,  
Charleston, S. C., June 26, 1982.



# SOCIOS NUEVOS

## ACTIVOS

**Carrión García, Enrique, M.D.** - Escuela de Medicina de la Universidad de Salamanca, España, 1970, Especialidad: Pediatría - Ejerce en Ponce.

**Cruz Burgos, Osvaldo, M.D.** - Escuela de Medicina de la Universidad de Santiago de Compostela, España, 1976, Especialidad: Pediatría - Ejerce en Luquillo.

**Díaz López, Gloria L., M.D.** - Escuela de Medicina de la Universidad de Valencia, España, 1974, Especialidad: Medicina de Emergencia - Ejerce en Santurce.

**Espinosa García, Mario E., M.D.** - Escuela de Medicina de la Universidad Autónoma de Santo Domingo, 1975, Especialidad: Neumología - Ejerce en Bayamón.

**González Rodríguez, Manuel A., M.D.** - Escuela de Medicina de la Universidad Santiago de Compostela, España 1971. Especialidad: Obstetricia y Ginecología - Ejerce en San Germán.

**Hernández Denton, Jorge, M.D.** - Escuela de Medicina de la Universidad de Yale en New Haven, Connecticut, 1973, Especialidad: Medicina Interna y Gastroenterología - Ejerce en Santurce.

**Marrero Arroyo, Carlos J., M.D.** - Escuela de Medicina de la Universidad Autónoma de Guadalajara, México, 1977, Especialidad: Obstetricia y Ginecología.

**Otero Hernández, Pedro A., M.D.** - Escuela de Medicina de la Universidad Autónoma de Santo Domingo, 1972, Especialidad: Obstetricia y Ginecología - Ejerce en Vega Alta.

**Polanco Reyes, Eladio A., M.D.** - Escuela de Medicina de la Universidad Autónoma de Santo Domingo, 1964, Medicina General - Ejerce en Carolina.

**Ramírez Ariza, Juan L., M.D.** - Escuela de Medicina de la Universidad de Sevilla, España, 1971, Especialidad: Obstetricia y Ginecología - Ejerce en Hato Rey.

**Ramírez Sánchez, Juan A., M.D.** - Escuela de Medicina de la Universidad Santiago de Compostela, España 1976. Especialidad: Cirugía General - Ejerce en Río Piedras.

**Rodríguez Noble, Juanita, M.D.** - Escuela de Medicina de la Universidad Pedro H. Ureña, República Dominicana, 1977. Especialidad: Pediatría - Ejerce en Bayamón.

**Roura Ortiz, Eugenio E., M.D.** - Escuela de Medicina de la Universidad Autónoma de Guadalajara, México, 1979, Medicina General - Ejerce en Río Piedras.

**Sánchez Ocasio, José F., M.D.** - Escuela de Medicina de la Universidad de Barcelona, España. Especialidad: Cirugía General - Ejerce en Ponce.

**Villar Robles, Félix M.D.** - Escuela de Medicina de la Universidad de Howard en Washington, D.C., 1973. Especialidad: Obstetricia y Ginecología - Ejerce en Bayamón.

**Zapata Guzmán, Víctor A., M.D.** - Escuela de Medicina de la Universidad Autónoma de Guadalajara, México, 1977, Medicina General - Ejerce en Bayamón.

## INTERNOS RESIDENTES

**Lao Sam, Florencio, M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1979, Residencia en Med. Física y Rehabilitación.

**Legarreta López, Juan F., M.D.** - Escuela de Medicina de la Universidad Central del Este de Santo Domingo, 1980.

## ESTUDIANTES DE MEDICINA

**Fernández Elicier, José F.** - Escuela de Medicina de la Universidad del Caribe de Cayey - Se graduará en 1984.

**Hernández Ortiz, Luis E.** - Escuela de Medicina de la Universidad Central del Este en Santo Domingo.

## REINGRESOS

**Cruz Rivera, Loida, M.D.** - Escuela de Medicina de la Universidad de Zaragoza, España, 1972, Especialidad - Pediatría - Ejerce en Bayamón.

**Meléndez Poventud, Luis H., M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1962, Especialidad: Medicina Interna - Ejerce en Río Piedras.

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## THE AMERICAN COLLEGE OF SPORTS MEDICINE

ACSM is a nonprofit, multi-disciplinary, professional and scientific society dedicated to the generation and dissemination of knowledge concerning the responses, adaptations, and clinical aspects of the human organism engaged in exercise and in recreational and competitive sport.

Our membership, representing over forty specialty areas, offers our members the opportunity for scientific exchange and inter-professional involvement. Over 9,000 individuals throughout the United States, Canada, and fifty other countries have found membership in the College to be a rewarding professional experience. Our international members are truly involved as demonstrated by the research presented in our scientific journal, *Medicine and Science in Sports and Exercise*, and in presentations at our annual meetings.

Membership in ACSM offers: educational opportunities, forums for presenting scientific research through meetings and publications, personal growth through contacts and friendships, and professional recognition through certification, awards, and advancement to Fellow.

### POSITION STANDS/OPINION STATEMENTS

As the leading organization in Sports Medicine, the College has published position stands and opinion statements dealing with specific topics of interest to the scientific and lay communities. The position stands have become accepted policy by rules committees throughout the United States and in foreign countries. Titles and dates of publication for ACSM Position Stands are:

- The Prevention of Heat Injuries During Distance Running (1975)
- Weight Loss in Wrestlers (1976).
- The Use and Abuse of Anabolic-Androgenic Steroids in Sports (1977).
- The Recommended Quantity and Quality of Exercise for Developing and Maintaining Fitness in Healthy Adults (1978).

An opinion statement is differentiated from a position stand in that it is considered to be the current state of the art or

science. One opinion statement has been published to date:

- The Participation of the Female Athlete in Long-Distance Running (1979).

Position stands currently being researched are: Marathon Running by Children; The Effects of Alcohol and Sports Participation; and Proper and Improper Weight Loss Techniques.

### MEMBERSHIP CATEGORIES

In the best interest of the purposes of the College, candidates are assigned to classifications that have different rights and privileges. Membership is on a calendar year basis (January to December).

There are four basic membership categories. However, in addition to these categories, members who have belonged to the College for at least three years, attended two annual meetings, and demonstrated their competence in sports medicine via publications or professional activities are eligible to apply for advancement to Fellowship status. A separate brochure on Fellowship is available upon request.

**Member.** Bachelor's, master's, or doctorate degree in a field related to health, physical education, exercise science or biology or a degree in another field and working in one of the above areas or equivalent to one of the above degrees and working in a related field (with a waiver of qualifications from the Credentials Committee).

**Graduate Student.** Bachelor's degree in a field related to health, physical education, exercise science, or biology and carrying at least one-half of a full academic load during one semester of the school year.

**Student Affiliate.** Full-time undergraduate in a field related to health, exercise science, biology, physical education, or the pre-medical sciences.

**Associate Member.** Open to any person with an interest in sports medicine who DOES NOT qualify for any other category.

Not all benefits and services apply to all categories.

### STATEMENT OF PURPOSE

The American College of Sports Medicine is a multi-disciplinary professional and scientific society dedicated to the generation and dissemination of knowledge concerning the responses, adaptations, and clinical aspects of the human organism engaged in exercise and in recreational and competitive sport.

The specific concerns are:

1. The basic physiological, biochemical, biomechanical, and behavioral mechanisms.
2. The improvement and maintenance of functional capacities for daily living.
3. The prevention and rehabilitation in chronic and degenerative disease.
4. The evaluation and conditioning of athletes.
5. The prevention and treatment of injuries.



## NATIONAL COUNCIL ON DRUGS

### USE OF APPROVED DRUGS FOR UNLABELED THERAPEUTIC PURPOSES

Federal law requires that the Food and Drug Administration approve the labeling for all marketed drugs and the indication for which they can be advertised or promoted. This labeling is intended to provide the information necessary for the drug to be used safely and effectively. It is based solely upon the data submitted to the FDA by the manufacturer.

After a drug has been marketed, information may come to light concerning its utility for purposes not included in the official FDA labeling. Most frequently, this new information relates to possible new clinical indications; it can also relate to new routes of administration, new dosage regimens, or use in age groups not covered in the original labeling. Questions frequently arise as to liability when a physician contemplates using a drug for one or more of these "unapproved" purposes. Indeed, legislative proposals have, in the past, been introduced that could impose penalties on physicians who prescribe drugs for any purpose not approved in the labeling.

It is the position of the National Council on Drugs that the use of an approved drug for "unapproved" (or unlabeled) purposes does not constitute an improper use and certainly not an illegal use. Drug labeling constrains a manufacturer as to permissible claims in advertising but is not designed to constrain the practice of medicine. Irrespective of the labeling status of a drug, the responsibility of a prescribing physician is the same—to decide what drug and dosage the patient will receive and for what purpose. The decision must be based upon rationale and reasonable medical evidence in the best interest of the patient. Thus the prescribing of an "unapproved" purpose requires only that the same judgment be exercised as is standards. This position is supported by the FDA as well as the health care professions.<sup>1</sup>

The National Council on Drugs recognizes that drug labeling lags behind accumulated knowledge concerning any given marketed agent. In some cases, drug labeling may never reflect the current status of a drug because there may not be sufficient incentive for a manufacturer to gather the requisite data needed to update the labeling. Thus, lack of labeling approval for a specific use should not preclude a physician from prescribing a marketed drug when this may be in the best interest of the patient. In the final analysis, it is accumulated professional experience—not labeling—that determines the ultimate and reasonable usage of a drug.

#### Reference:

1. American Academy of Pediatrics, Committee on Drugs: Unapproved Uses of Approved Drugs: The Physician, the Package Insert, and the FDA. Pediatrics 1978; 62:262-264.

### STANDARDS OF EVIDENCE FOR DRUG APPROVAL

As an answer to the question of drug safety, precipitated by the use of thalidomide in Europe, in August, 1962, Con-

gress passed the Harrison-Kefauver Drug Amendments that introduced government preapproval of new drug *efficacy*. Although a few critics offered a weak argument that such regulation was not really necessary, none seriously opposed the concept that drugs introduced into medical practice should have both safety and efficacy demonstrated prior to their commercial availability. The 1962 Amendments requires that "substantial evidence" of efficacy must be established for a new drug proposed for FDA approval. Today, some 18 years later, industry, academia, and government regulators are still quarreling about what constitutes "substantial evidence".

The original 1962 Amendments may have said it best of all: "The term 'substantial evidence' means evidence consisting of adequate and well-controlled investigations 'by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved', on the basis of which it could fairly and responsibly be concluded 'by such experts' that the drug will have the effect it purports or is represented to have 'under the conditions of use prescribed, recommended, or suggested in the labeling' or proposed labeling thereof." (See 505 (e), Federal Food, Drug and Cosmetic Act). (Single quotes added).

What has happened in the interim 18 years to confuse this simple goal? In regulatory-legal fashion, each word has been dissected and redissected until today the regulations that interpret and actually regulate this law into action often seem to bear little resemblance to the original intent and occasionally may even exceed the Congressional objective. A simple, straightforward statement of intent has been translated into a dozen paragraphs of medical-legal definition that is having an adverse impact on research and new drug approval. Today government bureaucrats—frequently not experts in medicine—determine with ever-increasing complexity and annoying vacillation the details of what, how, who, when, and where shall constitute "substantial evidence". Acknowledged medical experts can be overruled by unknown regulators, and only one way of conducting research and interpreting its results is acceptable—the government or FDA way. Regulatory Lysenkoism may be closer than we think.

The National Council on Drugs disagrees, not with the law, but with the legalistic interpretation of it by the FDA and calls upon Congress to re-examine this issue which is critical to the future of both medical research and medical therapeutics. The essentials of a rational scheme are not complex and the NCD suggests the following as a beginning:

1) As stated in the present law, demonstration of efficacy should be determined by medical experts who are known and respected by their peers for knowledge in the specific area, not by unknown bureaucrats behind closed doors. If it is the intent of the law that experts should make such judgments (and the National Council on Drugs agrees that they should), it is imperative that the current "conflict-of-interest" provisions, which equate drug knowledge and experience with bias, and ignorance of same with competence, must be modified.

2) Adequate, well-controlled trials may take many forms, and no one definition is necessarily applicable to all situations. It is the expert, not the data manipulators, who must be convinced. In short, it is the results of studies that should be convincing, not the ritual by which they are obtained.



(3) Finally, as the present law so wisely states, approval and the labeled use of a drug should be based upon the data accepted by known experts. The present regulatory policy of requiring evidence to support a predetermined concept of use and labeling is a major contribution to our present problem and probably was not intended by Congress.

In the opinion of the NCD, the issue of what constitutes adequate documentation of efficacy and safety is really intrinsic to many, if not most, problems with drug research and development regulation in this country. Congress should reaffirm its intended objectives before it is too late.



## THE DUET PROGRAM CAN PLAY A VITAL ROLE IN PATIENT EDUCATION

DUET is a new patient education program of the American Academy of Family Physicians. The acronym stands for "Drug Use Education Tips," a joint project of the AAFP and the U.S. Pharmacopeial Convention, Inc. (USP).

DUET is designed to help family doctors do a better job of informing their patients on the effects of drugs prescribed for them. This is done through use of a book called "Advice for the Patient," which is abstracted from the 1983 USP Dispensing information.

The book is written in easy-to-understand layman's language. Included is information on proper use, storage, side effects, precautions and interactions. Drugs appear under their generic names.

USP has granted permission for prescribers and dispensers to photocopy pages to give to patients for permanent reference.

"Advice for the Patient", along with a "how to" pamphlet to help physicians use it most effectively in their patient education programs, may be ordered direct from the AAFP. A poster for physicians' offices encouraging patients to "ask about your medicines" will be sent with each book.

Price of the DUET package to AAFP members is \$15.95. Send checks to the AAFP Order Department, 1740 W. 92nd St., Kansas City, Mo. 64114, or call the toll-free number, 1-800-821-2512, for further information.

The DUET project is under direction of the Academy's Committee on Drugs and Devices (formerly the Ad Hoc Task Force on FDA (Regulations).

"This is the best kind of patient education project," said Dr. Allan Bruckheim, chairman of the committee. "It is vital information immediately specific to the needs of the individual patient. It's a complete package covering all medications.

"Also, it has the authority of not only the individual's doctor but also the national standard-setting agency for drugs. It's a natural."



## BIRTHS INCREASE, INFANT DEATHS CONTINUE DECLINE

Infant deaths in the U.S. continued to decline between 1980 and 1981 to an estimated 42,700, a rate of 11.7 per 1,000 live births, compared with 12.5 in 1980, and the number of live births increased just over one percent to 3.6 million, according to a summary of health statistics in the December issue of *Pediatrics*, the journal of the American Academy of Pediatrics.

The summary was based on preliminary data gathered by the National Center for Health Statistics (NCHS) and the Statistical Office of the United Nations and written by Myron E. Wegman, M.D., FAAP, dean emeritus of the School of Public Health and professor of pediatrics emeritus in the Medical School of the University of Michigan, Ann Arbor.

The death rate for babies under one year of age in 1981 was less than half of what it was 20 years ago (26 deaths per 1,000 live births in 1960). The 1981 birth rate was 15.9 per 1,000 population.

None of the leading causes of death in infants increased in 1981. The leading causes that declined the most were respiratory distress syndrome, which fell from 139.8 per 100,000 live births to 116.0, and sudden infant death syndrome, which fell from 146.8 to 135.2.

In 1979 approximately 120,000 first births were to women age 30 and older, twice as many as in 1970, and the birth rate for women aged 30 to 44 increased 70 percent while the proportion of such women increased only about 20 percent. This reflected a gradually rising age at marriage and tendency to delay first births.

According to Dr. Wegman, if more women continue to have babies later in life, pediatricians may be concerned about a higher incidence of birth defects and low-birth weight infants. Yet, he notes, the proportion of first births with low birth weights declined between 1965 and 1979 for all age groups and especially for women 30 and older. Furthermore, women in all age groups with college educations had relatively fewer low-birth-weight infants.

The U.N.'s international data showed that, like the U.S., the other countries among the 25 with the lowest infant death rates all had continued declines in those rates, and more than one-third of them now have rates under 10 to 1,000 live births.

The U.S. ranks 18th on the list but the author notes that overconcern about small differences in very low infant mortality rates may stimulate "numbers competition" to achieve lower rates for their own sake, and the criticism by some health professionals that this competition may lead to disproportionate expenditures for high technology is well taken.

"It would seem better social policy", said Dr. Wegman, "to put emphasis on more and higher quality prenatal care and on preventive and primary care techniques for the infant and preschool child." Such a policy, he said, would not interfere with continued investigation into ways to save lives in the newborn period. He added that while the "dramatic decline" in infant mortality rates among developed countries "is commendable", the challenge is to provide public health protection and medical care to all children in the U.S.

## FAMILY STRESS MAY BOOST RISK OF CHILD'S ILLNESS

Children from families that undergo a great deal of stress may have an increased risk of suffering illnesses and accidents, according to an article in the December, 1982, issue of *Pediatrics*, the journal of the American Academy of Pediatrics.

The three-year project, conducted by a team at Christchurch Hospital in New Zealand, included 1,082 children from birth to age four. Rates of illness for six conditions were analyzed: illness of the lower respiratory tract, gastroenteritis, burns and scalds, accidental poisoning, other accidents, and suspect home-related conditions, such as child abuse.

The mothers also were asked annually whether one or more of 20 stressful events, such as death or illness of a close relative, financial problems, or marital problems, had taken place in the family.

It was found that children from families that had experien-

ced 12 or more of the events were twice as likely as were children from families with three or fewer events to have needed medical attention for the conditions included in the study.

The discrepancy was even greater for hospital admissions alone. Children from families with 12 or more stressful events were six times as likely to have been hospitalized as children from families with three or fewer events.

Statistical tests to determine whether the family's social background or standard of living was an underlying factor in the children's illnesses were performed. The results showed that the effects of these factors were negligible.

One explanation for the results is that stress in a child's family may decrease the mother's ability to cope, which may result in a "decrease in child rearing standards and a consequent increase in the risks of childhood morbidity." Another explanation, investigators said, was that stress physiologically might change the child's susceptibility to illness. The investigators said that most likely, both factors contributed to greater morbidity of children in families that undergo stress.

Fotografía cortesía de Dolores Méndez-Cashion, MD.



Exportando Ron y Melao para España. "En Ponce se hace mucho negocio con la exportación de ron y melao, también

pescado seco, que se embarcan en grandes cantidades hacia La Habana y otros puntos".





## CHOLESTEROL, CANCER LINK DISPUTED

Findings of an international group involving 11 independent studies in eight countries dispute recent reports linking low levels of cholesterol in the blood to the development of cancer.

Many previous studies raised the specter of a possible relationship between low blood cholesterol and cancer, though the findings were often inconsistent.

Results of the latest collaborative study, appearing in a December issue of the *Journal of the American Medical Association*, tend to link lower cholesterol levels in cancer victims with the effect of their disease rather than the other way around. The findings, the authors say, do not substantiate a hypothesis that low cholesterol increases the risk of cancer.

The study, which prominently involved the Department of Community Health and Preventive Medicine at Northwestern University Medical School under Jeremiah Stamler, MD, was based on information accumulated from 61,567 men aged 40 to 69 years.

Other countries involved in the study include Austria, Denmark, England, Finland, France, Japan and Scotland.

Although the collaborative study does not explain totally all the aspects of the cholesterol-cancer association, it does throw new doubt on any causative relationship of low cholesterol to cancer, writes Robert I Levy, MD, at Tufts University School of Medicine in Boston in an accompanying editorial.

Levy concludes on balance that the facts on hand still support a reduction of cholesterol and saturated fats in the American diet as a prudent step to reduce the amount of coronary heart disease in the United States.

## POTENTIAL SEEN FOR INTRAUTERINE SURGERY TO RELIEVE FETAL HYDROCEPHALUS

In another advance in intrauterine surgery, physicians from Harvard Medical School and Brigham and Women's Hospital, Boston, treated a 24-week fetus for hydrocephalus by implanting a shunt to continually drain excess fluids, according to a report in *JAMA*.

The procedure by Frederic D. Figoletto, Jr., MD, and colleagues has been called "the vanguard of pioneering efforts" in intrauterine surgery by Gordon B. Avery, MD, in an accompanying editorial in *JAMA*. But their work has prompted Avery, affiliated with the Children's Hospital at the

National Medical Center, Washington, DC, to develop some personal recommendations for physicians considering fetal surgery.

Physicians should first weigh all alternatives, writes Avery, and decide if there is reasonable chance for success. After the procedure is reviewed by other appropriately trained physicians, it should then be presented as an alternative to the parents, who should be clearly aware of its experimental status. Finally, he advises, all steps of the operation should be recorded for future reference.

"Fetal surgery represents an area of challenge and danger", writes Avery. "The challenge is to find new and effective ways to care for the fetal patient. The danger is that we will do more harm than good and will excessively intrude technology into the quiet and privileged sanctuary of the womb."

Hydrocephalus, produces an enlarged head in the fetus, forcing delivery by cesarean section. If not treated, the congenital disease can result in brain damage.

Figoletto and coauthors of the *JAMA* report implanted one end of a soft plastic tube or shunt into the left side of the fetal brain. The free end allowed excess fluid to drain safely out of the brain into the amniotic fluid that normally surrounds and cushions a fetus. Two weeks later, they placed another shunt on the right side. Subsequent examinations using ultrasound showed a decrease in the size of the fetal skull.

Fetal distress at 28 weeks gestation forced the physicians to perform an emergency cesarean section. The infant, born with other congenital abnormalities, suffered respiratory distress and a variety of medical complications. He died of cardiac arrest at five and one half weeks of age.

## AMERICAN ADULTS MAY BE INADEQUATELY IMMUNIZED AGAINST TETANUS AND DIPHTHERIA

A significant proportion of adult men and women in the United States may never have been adequately immunized against tetanus and diphtheria or their immunity may have waned, writes an Ohio pediatrician in the *Journal of the American Medical Association*.

"Women during their most active reproductive years and adults older than age 50 years are frequently inadequately immunized against tetanus", explains Martin G. Myers, MD, of Children's Hospital Medical Center, Cincinnati. More than half of those at greatest risk of exposure to diphtheria, such as hospital employees, may not be properly protected against the disease, Myers adds.

To study whether immunization is safe and effective for older children and adults, Myers administered a combined tetanus-diphtheria toxoid vaccine to 28 previously unimmunized children aged 6 to 18 years, and to 30 adults aged 19 to 58 years, all members of a rural Amish community of Iowa. After two injections, the entire group demonstrated a protective level of antibodies to tetanus and 94 percent of the individuals developed antibodies to diphtheria. In one child and two adults a protective level of antibodies to diphtheria was not reached until after the third injection.

Although the group experienced a relatively high rate of reactions to the vaccine, symptoms were mild consisting only of pain, tenderness and reddening at the injection site. Only one

man had systemic reactions of fever and headache, and these stopped before the third injection.

The incidence of tetanus and diphtheria have declined remarkably since immunization was introduced a half-century ago. However, the mortality rates associated with these diseases remain essentially unchanged, Myers says. According to the Centers for Disease Control in Atlanta, the death per case ratio for tetanus is 40 percent. For diphtheria, a less fatal disease, the ratio is nine percent.

Myers' data demonstrate that first-time immunization of older children and adults is safe and effective in evoking levels of antibodies considered to be protective.

## REVERSING STROKES

In a preliminary clinical study, a therapeutic technique to reverse a stroke before it has completely choked off blood to a region in the brain has been found effective in eight of nine patients treated by a neurosurgeon at Emory University Clinic in Atlanta.

The study, published in a December issue of JAMA, traces the improvement in patients who were experiencing such symptoms of strokes as partial paralysis or loss of speech. The improvement followed the administration during the early stages of a developing stroke of simple agents that dilute the blood.

The authors of the study, James H. Wood, MD, who is at Emory, and Alan S. Fleischer, MD, who is now with the University of Arizona School of Medicine in Tucson, suggests that the dilution technique works because it improves the flow of blood to the deprived area of the brain through what are called collateral blood vessels. These small collateral blood vessels do not come into play significantly unless the main arteries are narrowed or blocked off.

Although Wood and Fleischer's study lacked a control group, which in standard experimental design is the way comparisons can be made between those who receive new treatment and those who do not, the rate of improvement seen was greater than what would normally be expected in these patients, suggests John M. Hallenbeck, MD, of the Naval Medical Research Institute in Bethesda, MD. Hallenbeck, in an accompanying editorial, calls for additional studies.

## SHARP DROP NOTED IN A WOMAN'S RISK OF DEATH FROM LEGAL ABORTION

Deaths following legal abortion have fallen sharply since 1975 in contrast to maternal deaths during the nine months of pregnancy, which have declined at a slower pace, according to an analysis by the Centers for Disease Control (CDC) reported in JAMA.

The authors conclude that the risk of a healthy woman's dying from elective abortion is extremely rare. Women with chronic heart disease or other serious preexisting conditions, though, have a greatly increased risk regardless of whether they seek abortion or choose to carry the baby through to delivery. Even so, abortion is probably the safest option for these women, in terms of mortality risks, the authors say.

The analysis, presented in two articles, extends a study on data from 1972 through 1974 reported previously in JAMA. The current articles give a detailed breakdown of mortality statistics from abortion and childbirth through 1978 and rebut criticism that challenged the validity of the earlier study.

In their analysis of the data, the CDC investigators found that deaths after abortion fell from 3.2 per 100,000 abortions for the years 1972 through 1975 to 0.9 per 100,000 abortions for 1976 through 1978.

The number of maternal deaths fell from 12.6 per 100,000 live births in 1972 through 1975 to 9.3 per 100,000 live births in 1976 through 1978, according to figures cited in the report.

Data accumulated since 1975 corroborate the earlier finding that abortion is safer for the mother than childbirth in terms of risk of death, according to the study's principal author Willard Cates, Jr., MD, at the CDC in Atlanta. From 1972 through 1974, when the calculated risk of death from childbirth was five times greater than that from abortion, the gap in the relative risks widened to more than tenfold in the period 1976 through 1978.

In absolute numbers, rather than rates, 138 abortion-related deaths among women were reported from 1972 through 1978. During the same period, more than 7 million abortions were reported to have been performed. In 1978—the most recent year for which data are presented—there were seven deaths among women following abortion and 1.4 million abortions.

The count of abortion-related deaths was derived from information accumulated by the CDC's ongoing nationwide surveillance of abortion mortality. The count of abortions was derived from data reported by the Alan Guttmacher Institute.

The reported number of maternal deaths for the same seven years is 2,508; there were 22.5 million live births. In 1978 there were 268 maternal deaths and 3.3 million live births. These figures were derived from the national vital statistics system of the National Center for Health Statistics.

Such serious preexisting conditions as chronic heart disease, obesity and hypertension, among others, were noted to have jeopardized the health of 34 percent of the women who died after abortion in the study period. In lieu of reliable nationwide data on the prevalence of preexisting conditions among all women undergoing abortion from 1972 through 1978, the authors used data on the rates of preexisting conditions in women who sought abortion in hospitals or other facilities that participated in a study conducted by the CDC from 1971 through 1975.

Using this approach, they estimated that 1.3 percent of the women obtaining abortions between 1972 and 1978 had preexisting conditions that were dangerous enough to meet the criteria for therapeutic abortion.

If women with preexisting conditions are removed from the analysis, the authors note that the death-to-care rate for legal abortion is lowered considerably. In their calculations, the best estimate of the current risk of dying from legal abortion for healthy women in the United States is less than one per 100,000 procedures.

The CDC investigators also found that the death rates from abortion were lowest for women 19 years or younger and highest for women 35 years and older. Women of minority races (noted as black and other) had a mortality rate following either abortion or childbearing that was more than double that of white women. The lowest maternal mortality rate was



in women aged 20 to 24 years.

The authors believe that information on the safety of both elective abortion and childbirth may influence women who confront the often difficult choice between these two options.

## GENETICALLY ENGINEERED INTERFERON SHOWS ANTITUMOR ACTIVITY IN SOME HUMAN CANCERS

In the first trial to assess the effects of different doses of genetically engineered interferon, researchers found evidence of tumor regression in a variety of cancers according to a National Cancer Institute study in a November 1982 issue of JAMA.

This trial and others have paved the way for more definitive tests on the anticancer potential of interferon that are in progress.

According to the current JAMA report, the biosynthetic interferon had anticancer activity in patients with non-Hodgkin's lymphoma breast cancer, chronic lymphocytic leukemia, Hodgkin's disease and melanoma. The remissions lasted from three to seven months, writes Stephen A. Sherwin, MD, primary author of the NCI report.

A major part of the study—to assess the safety of the interferon—left researchers confident that the biosynthetic interferon not only works, but that it produces side effects no more difficult to handle than those which have been reported for natural interferon.

Since interferon was first described in 1957, more knowledge has been accumulated about it than about any other therapeutic agent previously studied in man, according to Stanford University's Thomas C. Merigan, MD, also writing in this week's JAMA. "Although one can gain insights quickly of whether or not interferon has biologic activity in clinical disease," he says, "the critical evaluation of how interferon compares with available chemotherapy—and whether it substantially alters the long-term course of disease—can be determined only after years of careful investigation."

Recombinant DNA techniques have ensured that enough interferon can be produced to investigate all of its therapeutic uses.

## DEBUNKING THE CHRISTMAS DEPRESSION SYNDROME

Is Christmas hazardous to your mental health? Many people think so. In fact, much of what we read about depression in the popular press concerns Christmas-time depression. Beat those holiday blues, the articles tell us, and they have case reports, helpful hints and comments from psychiatrists.

Hauling out discussions of the Christmas depression syndrome has become an annual custom somewhat like hauling out the decorations, singing carols and putting on Santa Claus suits. So say two University of Virginia Medical Center psychiatrists, who, after reviewing the subject, found that statistical studies do not support the conclusion that Christmas is hazardous to the public health.

"No measure of psychopathology in general, or of depression in particular, has ever shown a consistent increase before Christmas", write James Randolph Hillard, MD, and John Buchman, MD, in the December 17 *Journal of the American Medical Association*.

The authors have found that the number of suicides, psychiatric hospitalization and even letters to advice columns is relatively low during December, as compared with other months.

The pattern of prominent psychiatric illness declines, they say, during the days and weeks before Christmas and on Christmas Day itself. But they have found a rebound in January, when such illness swings back. A similar pattern has been found around other major holidays such as Easter and Independence Day, they say.

Why then the discrepancy between the high rate of Christmas depression postulated in popular articles or implied by the case report literature and the low rate found in statistical studies?

For one thing, they say, the number of people who become severely depressed around Christmas is not large enough to affect public health statistics. They admit that the Christmas season can unleash a variety of emotions and conflicts, from feelings of self-indulgence or wish fulfillment followed by frustration to increased demands for money or increased pressure to interact with relatives. But they say that few people actually fail to cope with such stresses.

Hillard and Buckman suggest that perhaps too little attention has been given to the positive psychological and social effect of Christmas. The support from friends and relatives and the increased sense of hope during the season can help get people through despite the stresses, they say.

Look to the positive, they advise, for boosting feelings of continuity with family, community, the past and the future. Avoid unrealistic expectations of solutions to personal or family problems. And keep in mind that what is good health advice the rest of the year is also good during the holidays—in other words, moderation in food, alcohol and social commitments in prudent.



## EDUCACION MEDICA CONTINUADA

TENTH ANNUAL PEDIATRIC SYMPOSIUM  
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MEDICAL CENTER  
WASHINGTON, D.C.

in conjunction with the  
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Presenta

### Seminario HIPNOSIS CLINICA

5 Créditos Categoría I

Seminario auspiciado por el Ashford Memorial Community  
Center, Institución aprobada por la Asociación Médica de  
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Seminario incluye:

- Introducción a la hipnosis
- Historia de la Hipnosis
- Ejercicios a nivel de hipnosis colectiva
  - A- Levitación de mano
  - B- Balanceo Postural
- Técnicas de hipnosis a niveles individuales
- Demostración de inducciones hipnóticas a niveles indivi-  
duales
- Técnicas y usos de auto-hipnosis (aplicada para el  
mejoramiento personal.)
- Estados Anestésicos - Hipnoanestesia  
Demostración y provocación de estados anestésicos
- Estados Regresivos  
Técnicas y demostración de regresión en el tiempo
- Hipnosis clínica y sus aplicaciones en las diversas áreas de  
las especialidades médicas
- Sesión de panel - Preguntas y Respuestas

CONFERENCIANTES: Nelson Salazar Cummings, Psicó-  
logo Clínico, Frank Rodríguez Martínez, M.D.

FECHA: Sábado 29 de enero de 1983

LUGAR: Sala de conferencia Hospital Ashford Memorial  
Community Center

HORARIO: De 10:00 a.m. a 4:00 p.m.

COSTO: \$65.00. Incluye almuerzo de 12:30 a 1:30

INTERESADOS DEBEN SEPARAR ASIENTO: Depósito  
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INFORMACION ADICIONAL: Centro Clínico Hipnotera-  
peutico, Condominio Las Torres - Norte, Oficina 6-A, Baya-  
món, Puerto Rico 00619. Tel. 798-1429



## MEETINGS IN THE UNITED STATES

February 1983

**American College of Emergency Physicians, Surgery/Trauma**, Westin Hotel, Detroit, Feb. 8-12; Inf. ACEP, PO Box 61911, Dallas, TX 75261.

**American College of Psychiatrists**, New Orleans Hilton, New Orleans, Feb. 16-20. Sec. Gen: H.H. Work, MD, 1700 18th St, NW, Washington, DC 20009.

**Cardiac Auscultation**, sponsored by SUNYB and the Cardiac Study Fund, Sheraton of Boca Raton, Boca Raton, Fla, Feb 21-23. Inf. G. Myers, Box 14, Hiler Branch, Buffalo, NY 14223.

**Cleveland Clinic/University of Vermont Sports Medicine Symposium for Family Practitioners, Orthopaedic Surgeons and other Allied Health Personnel**, Sugarbush, Vt, Feb 13-18. Inf. J.A. Bergfeld, MD, Head, Section Sports Med, Dept Orthopaedic Surgery, Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44106.

**Current Concepts in Ophthalmology-Retina, Vitreous, Glaucoma & Pediatrics**, sponsored by Florida Midwinter Seminar in Ophthalmology and Otolaryngology, Hyatt Hotel, Palm Beach, Fla, Feb 14-16. Inf. Florida Midwinter Seminar, 405 Northeast 144 St, Miami, FL 33161.

**John R. Durrance Mid-Winter Chest Conference**, Aspen Meadows, Aspen, Colo, Feb 9-12. Inf. American Lung Association, PO Box 921, Loveland, CO 80537.

**International Academy of Pathology United States-Canadian Division**, Atlanta Hilton, Atlanta, Feb 26-March 4. Sec-Treas: N. Kaufman, MD, 1003 Chafee Ave, Augusta, GA 30904.

**International Conference of the Association for Children and Adults With Learning Disabilities (20th)**, Washington, DC, Hilton, Washington, DC, Feb 16-19. Exec Dir: J. Petersen, National ACLD, Inc., 4156 Library RD, Pittsburgh, PA 15234.

**International Workshop Neurological Surgery of the Ear and Skull Base**, Sarasota Hyatt House, Sarasota, Fla, Feb 19-24. Inf. H. Silverstein, MD, 1921 Floyd St, Sarasota, FL 33579.

**Orthopedic Pathology**, sponsored by the American Registry of Pathology and Armed Forces Institute of Pathology, Washington, DC, Feb 7-12. Inf. Am Registry of Pathology, Rm 1111, AFIP, Washington, DC 20306.

**Teaching Conference in Clinical Cardiology (15th)**, sponsored by Univ of Miami School of Med, and the Council on Clinical Cardiology of the American heart Association, Sheraton Bal Harbour Hotel, Bal Harbour, Fla, March 2-5. Inf. M.S. Gordon, MD, Univ of Miami School of Med, med Training and Stimulation Lab (D41), PO Box 016960, Miami, FL 33101.

**Otolaryngology-Head and Neck Surgery Update**, sponsored by Florida Midwinter Seminar in Ophthalmology and Otolaryngology, Hyatt Hotel, Palm Beach, Fla, Feb 17-19. Inf.

Florida Midwinter Seminar, 405 Northeast 144 St, Miami, FL 33161.

**Pediatric Infectious Disease Seminar**, Las Vegas Hilton Hotel, Las Vegas, Feb 17-19. Inf. G.H. McCracken, Jr, MD, Univ of Texas health Science Center at Dallas, 5323 Harry Hines Blvd, Dallas, TX 75235.

**Sports Medicine in Primary Care**, sponsored by New England Chapter, American College of Sports Medicine, and Services of Sports Medicine, Waterville Valley Conference Center, Waterville Valley, NH, Feb 13-18. Inf. R.C. Cantu, Neurological Surgery, Level 4, Cuming Building, Concord, MS 01742.

**Tutorial in Cardiology (5th)**, Surgerbush Inn, Warren, Vt, Feb 28-March 4. Inf. P. Wright, Cardiology, Mary Fletcher Unit, Burlington, VT 05401.

## March 1983

**American Academy of Allergy, Diplomats**, Miami, March 19-23. Exec Dir: D.L. McNeil, 611 E Wells St, Milwaukee, WI 53202.

**American Academy of Orthopedic Surgeons**, Convention Center, Anaheim, Calif, March 10-15. Exec Dir: C.V. Heck, MD, AAOS, 444 N Michigan Ave, Suite 1500, Chicago, IL 60611.

**American College of Cardiology**, New Orleans, March 20-24. Exec Dir: W.D. Nelligan, CAE, 9111 Old Georgetown Rd, Bethesda, MD 20814.

**American College of Nuclear Physicians**, Cerromar Beach Hotel, Cerromar Beach, Puerto Rico, March 9-13. Exec Dir: C.A. Lively, 1101 Connecticut Ave, NW, Washington, DC 20036.

**American Psychosomatic Society**, Barbizon Plaza, New York City, March 24-27. Inf. B.F. Engel, PhD, 265 Nassau RD, Roosevelt, NY 11575.

**American Society of Abdominal Surgeons**, National Study Center for CME, Tampa, Fla, March 19-22. Exec. Sec: B.F. Alfano, MD, 675 Main St, Melrose, MA 02176.

**American Society for Clinical Pharmacology and Therapeutics**, Town & Country, San Diego, March 9-11. Sec-Treas: E.H. Funk, Jr, MD, 1718 Gallagher Rd, Norristown, PA 19401.

**American Society of Contemporary Medicine and Surgery**, Sheraton Bal Harbour Hotel, Bal Harbour, Fla, March 6-12. Dir: J.G. Bellows, MD, 211 E Chicago Ave, Suite 1044, Chicago, IL 60611.

**American Society of Contemporary Ophthalmology**, Sheraton Bal Harbour Hotel, Bal Harbour, Fla, March 5-12. Dir: J.G. Bellows, MD, 211 E Chicago Ave, Suite 1044, Chicago, IL 60611.

**American Society for Head & Neck Surgery**, Canyon, Palm Springs, Nev, March 10-13. Sec. W.E. Fee, Jr, MD, Div of Oto, Stanford Univ Med Center, Stanford, CA 94305.

## ¿QUE ES LA ASOCIACION MEDICA DE PUERTO RICO?

Es una asociación profesional voluntaria integrada por médicos. Se sostiene a través de las cuotas que pagan sus 2,500 socios. Tiene un personal administrativo no médico de alrededor de 17 personas.

Está dividida en seis Sociedades de Distrito, a saber: Este (con sede en San Juan), Sur (con sede en Ponce), Occidental (con sede en Mayagüez), Central (con sede en Caguas, Norte (con sede en Arecibo) y la Noreste, creada en 1982 con sede en Bayamón. Está afiliada además a la Asociación Médica Americana.

La Asociación persigue el mejorar la salud y el bienestar de todo el pueblo. A través de la prensa, radio, televisión y material impreso, trata de orientar al pueblo en lo referente a

un mejor cuidado de la salud. En cooperación tanto con las agencias gubernamentales como privadas, la Asociación vela por el bienestar de la comunidad, brindando su cooperación en campañas o actividades en beneficio de la salud de todo el pueblo. Impulsa o combate cualquier legislación estatal o federal si de acuerdo con sus principios ha de ser ésta favorable o nociva a la comunidad. Mantiene a los médicos informados de los programas científicos, a través de publicaciones, cursos post-graduados y seminarios, de manera que los pacientes se beneficien lo más pronto posible de los últimos descubrimientos aprobados.

A pesar de que la AMPR está constituida por médicos, la misma se creó para servir tanto al público como a la profesión. Sus múltiples actividades benefician a ambos.

Fotografía cortesía de Dolores Méndez-Cashion, M.D.



*Coamo. Existen en varias partes manantiales calientes minerales de gran valor medicinal. Los mejores conocidos son los de Coamo, en la Carretera Nacional hacia San Juan, a poca distancia de Ponce, al noreste. Estos manantiales constituyen un reconocido lugar de curación visitado por inválidos de todas partes del mundo.*

*El calce de la foto dice: "aquí vemos el viejo Hotel Español en*

*los Baños de Coamo. Este lugar queda como a 6 millas del pueblo de Coamo, y era anteriormente un gran lugar de temporada para los españoles ricos, muchos de los cuales vienen de la vieja patria a recibir el beneficio de las aguas medicinales. Este hotel lo compró recientemente una compañía americana, con la intención de hacer mejorías extensas y establecer aquí un lugar de invernación.*



# BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

ORGANO OFICIAL



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ENERO A DICIEMBRE DE 1982

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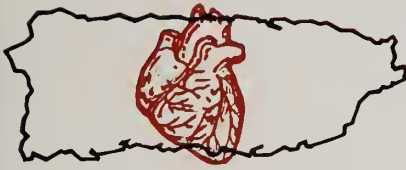


# 1er CONGRESO PUERTORRIQUEÑO DE CARDIOLOGIA

San Juan , 7 al 10 de abril de 1983.

Apartado Postal 5067 San Juan , Puerto Rico 00936

Telefonos : 753-3829 - 753-3830 - 763-7349



SOCIEDAD PUERTORRIQUEÑA DE CARDIOLOGIA  
ASOCIACION PUERTORRIQUEÑA DEL CORAZON  
ASOCIACION CARDIOVASCULAR DEL SUR  
COLEGIO AMERICANO DE CARDIOLOGIA, CAPITULO DE PUERTO RICO  
SECCION DE CARDIOLOGIA, ASOCIACION MEDICA DE PUERTO RICO  
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Con sumo placer queremos anunciar que los días 7, 8, 9 y 10 de abril de 1983, se celebrará en el Hotel Condado Holiday Inn el Primer Congreso Puertorriqueño de Cardiología.

A esta actividad científica, auspiciada por todas las Sociedades de Cardiología del país, y por la Escuela de Medicina de la Universidad de Puerto Rico, se darán cita distinguidos invitados de fama internacional y cardiólogos locales para discutir los más recientes adelantos en el diagnóstico y manejo de las enfermedades cardiovasculares de adultos y niños.

Entre los temas a discutirse se han seleccionado los de más relevancia en la práctica diaria, como: Enfermedad Coronaria, Muerte Súbita, Hipertensión Arterial, Marcapasos, Arritmias y Agentes Antiarrítmicos, Farmacoterapia Cardiovascular, Enfermedades Valvulares, Fallo Cardíaco, Enfermedades Congénitas, y otras enfermedades con que comúnmente se confronta el médico en su práctica diaria.

Este evento científico ha sido diseñado de tal manera para que sea de utilidad para Cardiólogos, Internistas, Cirujanos Cardiovasculares, Médicos de Familia y Generalistas.

Gracias a los patrocinadores, esta actividad educativa se ofrecerá a un precio módico para que se beneficie el mayor número de médicos de la comunidad. Los asistentes al curso recibirán 20 horas crédito en Categoría I.

Próximamente recibirán más información sobre esta histórica actividad, esperamos reserven la fecha en su calendario.

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# ASOCIACION MEDICA DE PUERTO RICO

# BOLETIN

## INSTRUCCIONES PARA LOS AUTORES

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuerzen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

### Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquina a doble espacio; por un solo lado de cada página, en TRIPPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

### Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

### Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

### Ilustraciones

Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor. Debe indicarse en la parte superior de la ilustración.

### Resumen

Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

### Referencias

Las referencias deben ser numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

1. Para artículos de revistas: *Apellido(s) e iniciales del nombre del autor(es), título del artículo, nombre de la revista, año volumen, número, páginas. Por ejemplo:*  
Villavicencio R: Soplos Inocentes en Pediatría. Bol. Asoc. Med. PR 1981; 73 (10): 479-87

Si hay más de 5 autores, incluir los primeros 3 y añadir et al.

2. Para citación de libros donde el autor(es) del capítulo citado es a su vez el (los) editor(es): *Apellido(s) e iniciales del autor(es), título del libro, número de edición, ciudad, cosa editora, año y página. Por ejemplo:*  
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Observar que no se usa el punto después de las iniciales de los autores ni al final de las referencias.

### Cartas al Editor

Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquina a doble espacio, no deben ser mayor de 500 palabras, ni incluir más de cinco referencias.

## INSTRUCTIONS TO AUTHORS

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

### Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

### Nomenclature

Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially).

### Tables

These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

### Figures

Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

### Summary

An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

### References

These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text.

1. For periodicals: *Surname and initials of author(s), title of article, name of journal, year, volume, pages. For example:*  
Villavicencio R.: Soplos Inocentes en Pediatría. Bol. Asoc. Med. PR 1981; 73 (10): 479-87

If there are more than 5 authors list only 3 and add et al.

2. For books when the author of the cited chapter is at the same time the editor: *Surname and initials of author(s), title, edition, city, publishing house, year and page. For example:*  
Keith JD, Rowe RD, Vlad P: Heart Disease in Infancy and Childhood, 3d Ed., New York, MacMillan, 1978, p. 789

3. For chapter in book when the author of the chapter is not one of the editors: *Olley PM: Cardiac Arrhythmias. In: Keith JD, Rowe RD, Vlad P. Heart Disease in Infancy and Childhood. 3d Ed, New York, MacMillan, 1978, 275-301*

Please note that the period is omitted after the author's initials and at the end of the references.

### Letters to the Editor

Will be published at the discretion of the Editorial Board. They should be typewritten double-spaced, should not exceed 500 words nor more than five references.

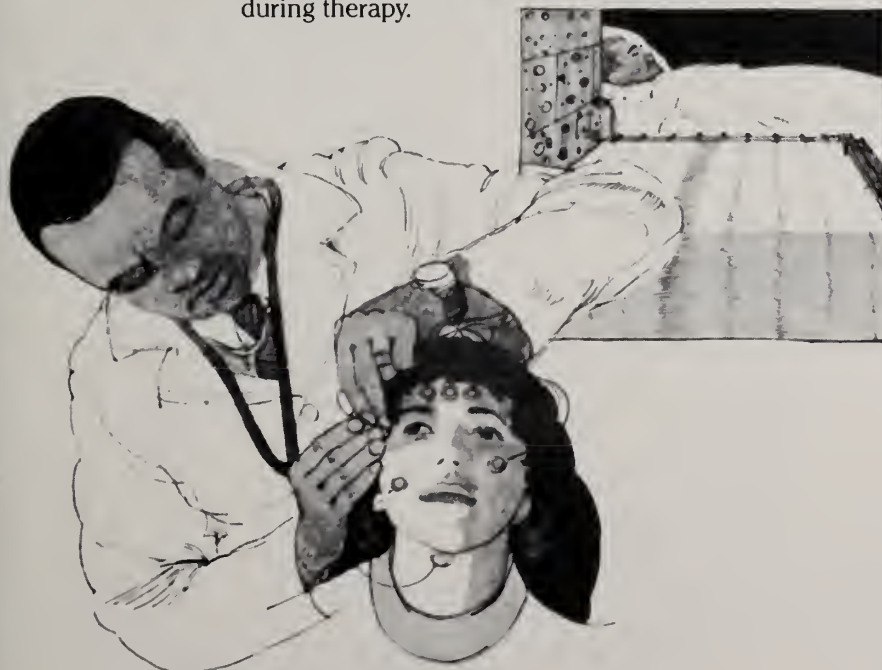


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sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington, DC, May 3-7, 1971. 12. Pollak CP, McGregor PA, Weitzman ED: The effects of flurazepam on daytime sleep after acute sleep-wake cycle reversal. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, June 30-July 4, 1975. 13. Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

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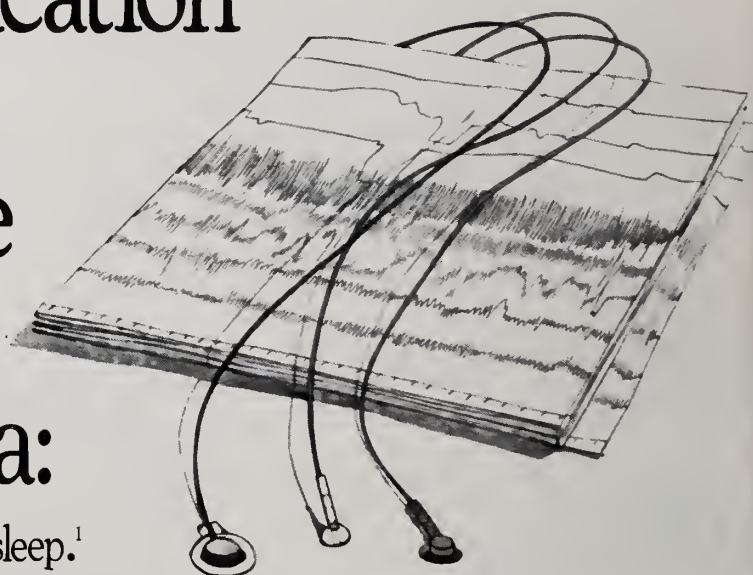
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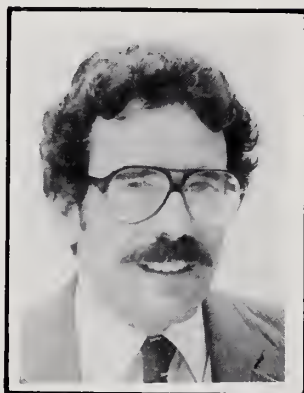
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## Columna del Editor



Con este número confiamos se inicie una nueva época en nuestra revista ya que esperamos que el papel a utilizarse sea "cromado". Este detalle permitirá una reproducción adecuada de radiografías, fotografías, y otras ilustraciones que en el pasado y por la pobre calidad del papel era frustrante su publicación. La Junta Editora cree que nuestro órgano oficial y nuestros lectores se lo merecen y a su vez motivará a autores potenciales a enviarnos sus trabajos para publicación. Esperamos que nuestra solicitud sea complacida por la Junta de Directores de nuestra Asociación.

Este número está encabezado por dos Editoriales de gran relevancia, uno sobre la especialidad de Cirugía Pediátrica y otro en relación al Deporte del Boxeo motivado por una carta del editor del *Journal of the American Medical Association* donde prácticamente se aboga por la suspensión de dicho deporte. Reproducimos la carta en la sección de Artículos Especiales y el Dr. Amaury Capella, Cirujano de vasta experiencia en este deporte nos deja saber sus opinión.

Además de los estudios clínicos de nuestros investigadores locales publicamos un artículo de un distinguido profesor austriaco, el Dr. W. Russe, sobre la rehabilitación de pacientes que han recibido tratamiento por tumores del hueso. Está excelentemente ilustrado.

Luego de dos años de publicación mensual ininterrumpida aparece el último caso de Electrocardiografía Pediátrica. Esperamos que haya cumplido su misión y estaremos alerta para la publicación de algún trazado de interés que encontremos en la práctica diaria de Cardiología Pediátrica para divulgarlo de la misma forma que se ha hecho por los últimos dos

años. Las fotografías antiguas también se han agotado. Si algún lector aficionado a la fotografía tiene fotos que desee publicar puede enviarla a la Asociación. Las mismas serán sometidas a la Junta Editora previa publicación y al calce de cada foto se identificará su autor. Esta idea fue sometida por el Dr. Miguel Colón Morales y aprobada por la Junta Editora. Esperamos la cooperación de la matrícula para que nos sometan material fotográfico de calidad para publicación.

A handwritten signature in dark ink, appearing to read 'Rafael Villavicencio'.

Rafael Villavicencio, M.D.  
Presidente Junta Editora  
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ASOCIACION MEDICA DE PUERTO RICO

## BOLETIN



VOL. 75/NUM. 2

FEBRERO 1983

### NUESTRA PORTADA:

"Cafetería Bayamón", óleo de 4' x 3' del artista puertorriqueño Carlos Dávila Rinaldi. El lugar existe, está ubicado en la Calle Loíza de Santurce, muy cerca del taller del autor. Para ello el artista iba todas las tardes a las 3:30 p.m. a dibujar los efectos de la luz, que es uno de los elementos más importantes de la obra. En ella se mezclan elementos reales y abstractos con una armonía extraordinaria. En los dibujos preliminares el artista había propuesto figuras dentro de la composición que luego fueron eliminadas porque le quitaba el efecto de soledad y tranquilidad de la obra. La obra hubo que pintarla dos veces pues la primera ocasión al barnizarla se dañó y el artista la cortó con una navaja. La restauración le tomó dos meses.

El autor es nacido en Santurce en 1958, en la adolescencia comenzó sus estudios de arte con los profesores García-Segovia y Luis Cajigas. A los 18 años se trasladó a Nueva York y continúa estudios con Louis Lieberman y Robert Stackhouse. En 1980 recibe su Bachillerato en Artes de la Universidad De Pauw en Indiana.

Desde 1979 sus construcciones, dibujos y óleos figuran en las principales Galerías del país, incluyendo una exposición individual en la Alcaldía de San Juan. En 1982 su obra fue expuesta en la Universidad de Puerto Rico bajo los auspicios de la UNESCO. En el mismo año su obra recibió un 2º premio en la categoría de pinturas en el certamen Mobil-Caribe.

El autor nos informa que después de dos años trabajando en construcciones y pinturas abstractas su trabajo ha dado un cambio hacia lo figurativo, mezclando lo real con lo abstracto y con lo expresionista. En sus trabajos vemos una simplificación de formas que se realizan en un patrón de formas negativas y positivas.

La "Cafetería Bayamón" pertenece a la colección privada del Sr. Andrés Marrero, propietario de Taller-Galería André en el Condominio El Centro en Hato Rey por cuya gentileza hemos podido reproducir la obra en nuestra portada.

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# EDITORIALES



## La Muerte Dentro y Fuera del Cuadrilátero

Se habla, se escribe y editorializa sobre abolir el boxeo cada vez que ocurre una muerte como resultado de un combate. Estamos pasando por una de esas etapas. Como médicos y miembros responsables de una sociedad tenemos por necesidad que preocuparnos.

Se argumenta que aunque el boxeo está octavo entre los deportes como causa de muerte a base de número de participantes, y a pesar de que en otros más peligrosos en ese sentido como el fútbol americano se golpea a veces causando inconciencia, en el pugilismo la intención primordial es causar daño corporal al contrario y deliberadamente producir inconciencia. Se alude además a la reciente evidencia tomográfica de atrofia cerebral en el síndrome de encefalopatía crónica post-traumática o demencia pugilística ("punch-drunk" syndrome).

Todo lo mencionado nos hace reflexionar sobre nuestras experiencias locales con ese deporte. Durante los últimos veinte años hemos estado íntimamente vinculados al boxeo profesional (no así al aficionado sobre el cual no comentaremos pues) en Puerto Rico. A lo largo de esas dos décadas se expidieron en nuestra isla más de 1,500 licencias a boxeadores profesionales y Puerto Rico se convirtió en una de las plazas más importantes para dicho deporte, produciendo diez campeones mundiales. Durante ese tiempo sin embargo, no ha habido que lamentar una sola muerte como resultado de golpes recibidos durante combates de boxeo profesional.

Nuestros requisitos de salud para otorgar una licencia profesional a un boxeador están entre las más estrictos del mundo y nuestros árbitros merecen gran crédito por haber siempre solicitado, oído y seguido nuestras recomendaciones médicas. El récord limpio de que nos enorgullecemos debe ser en gran parte un tributo a estos hombres. Tenemos casos de encefalopatía, pero al igual que la mayor parte de aquellos citados en la literatura, son producto de otras épocas, cuando no se protegía al boxeador en la medida que se ha venido haciendo desde entonces. Durante esa veintena solo tenemos

conocimiento de dos a quienes se le pueda otorgar como tales casos.

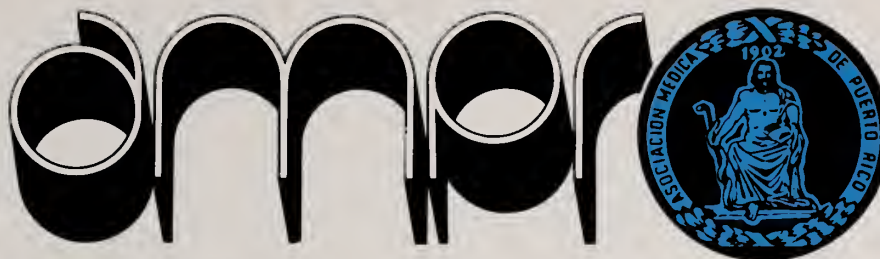
Un dato poco conocido es que durante esos veinte años, mientras ningún boxeador ha muerto como resultado de golpes recibidos dentro del cuadrilátero, varios han perdido sus vidas violentamente fuera de las doce cuerdas. Entre las circunstancias en que sucumbieron estos boxeadores puertorriqueños, o radicados en nuestra tierra, recordamos: suicidio por ahorca (Lasalle), asesinato por disparos (Ortiz, Bonavena), asesinato por puñaladas (Cabrera), sobredosis de droga (Bezares) y accidente automovilístico (Rodríguez). Una incidencia de muerte sumamente alta para adultos jóvenes, extremadamente saludables y entre los veinte años de edad; una prueba del trasfondo económico, social y cultural de estos jóvenes, la mayor parte procedente de nuestras clases menos privilegiadas, muchos de arrabales.

Crecen luchando a golpes por la vida, desarrollan rencores y hostilidad dentro de un ambiente de violencia. Encuentran en el deporte un escape para exteriorizar su agresividad de la única manera que la vida les enseñó: físicamente. Aprenden técnica. Unos meramente se ganan el sustento. Los escogidos alcanzan fama y fortuna nunca antes soñadas.

El boxeo profesional crea empleos y aleja estos jóvenes de su frecuentemente trágico medioambiente, encontrando refugio y aprendiendo disciplina en los gimnasios. Indiscutiblemente que entendemos el que se critique un deporte cuya finalidad es golpear al contrario. Abolir el boxeo sin embargo va a ser muy difícil, especialmente en una sociedad con una tasa alta de desempleo y crimen. Después de todo... las estadísticas demuestran que hay más peligro de muerte al caminar en la noche por las calles de San Juan que boxear profesionalmente en nuestros cuadriláteros.

Amaury Capella, M.D., F.A.C.S.  
Febrero 1983.





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# La Cirugía Pediátrica - 1983 -

A principios del siglo veinte no existe una disciplina específica para la cirugía pediátrica. No es hasta el 1908 cuando se nombra al Dr. William E. Ladd como facultativo del Boston Children's Hospital que comienza la temprana definición de esta especialidad. Ya para el 1914 el Dr. Ladd se ha dedicado total y exclusivamente al cuidado del paciente quirúrgico pediátrico. Comienza a adiestrar de manera personal a varios residentes que luego se establecen como cirujanos dedicados exclusivamente a niños. Basado en los esfuerzos de estos pioneros, y a pesar del escepticismo y la crítica de muchos, se comienza a laborar para establecer una nueva especialidad quirúrgica.

En 1941, por primera vez en una universidad norteamericana, se crea una plaza exclusiva para cirugía pediátrica, cuando la Escuela de Medicina de Harvard establece el "Ladd Professorship of Child Surgery". Para el 1941, la Academia Americana de Pediatría establece una sección quirúrgica con 20 miembros fundadores que definen como mínimo una práctica basada en 90% o más de tratamiento directo al paciente pediátrico. En el 1970 se forma el "American Pediatric Surgical Association" con 200 miembros fundadores. Esta asociación recibe la aprobación del "American Board of Medical Specialists" para la creación de una junta de cirugía pediátrica como subespecialidad de la Junta Americana de Cirugía (American Board of Surgery). Para el 1975, en Dorado, Puerto Rico, se administran los primeros exámenes de certificación especial en cirugía pediátrica. Subsiguientemente, el American Pediatric Surgical Association desarrolla criterios básicos para programas de adiestramiento en los centros de cirugía pediátrica y al presente autoriza a 18 centros en los Estados Unidos y Canadá para adiestramiento formal en esta subespecialidad.

Desde el 1981 la Junta Examinadora de Cirugía (American Board of Surgery) requiere como indispensable para tomar los exámenes, un entrenamiento formal en cirugía pediátrica en uno de los centros aprobados. Como requisito para este entrenamiento de cirugía pediátrica se necesita previo adiestramiento completo en el área de cirugía general, y para la certificación de cirugía pediátrica se requiere haber aprobado los dos exámenes (escrito y oral) de American Board of Surgery y ser certificado por la Junta en cirugía general. Al presente existen en Estados Unidos y Canadá 423 cirujanos pediátricos certificados por el American Board of Surgery. Los cirujanos pediátricos constituyen el uno por ciento de la membresía del Colegio Americano de Cirujanos.

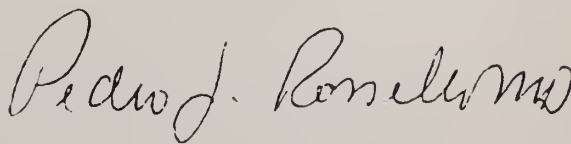
Concomitantemente con este crecimiento y formalización de la cirugía pediátrica, se documenta una mejoría en los resultados del tratamiento de las enfermedades pediátrico-quirúrgicas. Santulli en su ponencia presidencial ante el American Pediatric Surgical Association repasa el progreso en el tratamiento de estas condiciones, en particular de los llamados casos índices (atresia de esófago, omfalocele y gastros-

quisis, ano imperforado, hernia diafragmática, enfermedad de Hirschsprung, rhabdomyosarcoma, tumor de Wilms y neuroblastoma).<sup>2</sup>

En Puerto Rico, la cirugía pediátrica se desarrolla con un curso paralelo pero con un punto de partida más tardío. En sus inicios se puede constatar el trabajo pionero de un grupo de cirujanos generales que toman un interés específico en las enfermedades quirúrgicas en niños. Al presente contamos con tres cirujanos con certificación especial en cirugía pediátrica, dedicados al tratamiento exclusivo de niños. Basado en estudios hechos en Estados Unidos, podemos proyectar que existe campo en Puerto Rico para la participación de más cirujanos pediátricos. O'Neill, en un estudio sobre las necesidades para cirugía pediátrica a nivel nacional, encontró que existen hoy en los Estados Unidos cirujanos pediátricos en cada una de 62 áreas metropolitanas con población de más de 200,000.<sup>2</sup> Tomando el número de operaciones promedio del cirujano pediátrico y general, Holder estima que este número de cirujanos pediátricos en Estados Unidos es apropiado para la presente demanda.<sup>3</sup>

Por otro lado, es claro que el progreso en los resultados del tratamiento de las condiciones pediátrico-quirúrgicas requieren no solo al cirujano pediátrico bien adiestrado, sino también facilidades hospitalarias apropiadas para este nivel de cuidado y el apoyo de otros especialistas pediátricos competentes. Hemos llegado al momento donde las condiciones complejas de cirugía neonatal, cirugía oncológica y cirugía de trauma en niños deben tratarse solamente en aquellos centros que cuenten con las facilidades y el personal capacitado para ofrecer este tratamiento óptimo al niño. Se ha comprobado que existe una fuerte correlación entre el número de procedimientos quirúrgicos para una condición específica que se lleva a cabo en una institución y las tasas de mortalidad.<sup>4</sup> Considerando que los casos índices mencionados para cirugía pediátrica son relativamente infrecuentes, es claro que una estrategia lógica para mejorar resultados es concentrar el tratamiento de estos a centros designados para este propósito. El mismo argumento se puede aplicar a la organización de servicios de cirugía cardíaca y oncológica.

Ubiñas y otros en el artículo que aparece en esta edición del Boletín, presentan evidencia que apoya las ventajas del tratamiento de atresia de esófago y fístulas traqueoesofágicas en centros especializados en cirugía pediátrica.<sup>5</sup> Aunque la mayoría de los otros procedimientos no índice, con mayor frecuencia en la población, tales como piloromiotomía, reparación de hernias y apendectomías en niños pueden ser tratados adecuadamente en nuestros hospitales comunitarios y de área, creemos que la mejoría en el tratamiento de las condiciones índices depende de que estos sean tratados en su totalidad en instituciones designadas y habilitadas como Centros de Cirugía Pediátrica.



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# ESTUDIOS CLINICOS

## Esophageal Atresia and Tracheoesophageal Fistula at the Ponce Regional Hospital

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**Summary:** A retrospective study of cases with esophageal atresia and/or tracheoesophageal fistula diagnosed and treated at the Ponce Regional Hospital during the period 1969 to 1981 was carried out. The survival rates in this condition improved from 16.6% between 1969-71 to 66.6% from 1973-81. This temporal trend parallels that reported from other institutions, outside Puerto Rico, where presently levels of over 90% survival are achievable.

Esophageal atresia and tracheoesophageal fistula includes a spectrum of embryologically-determined abnormalities important in the field of pediatric surgery. The incidence of these malformation in the United States is approximately 1.6 cases per ten thousand live births.<sup>1</sup> Based on these figures, Puerto Rico would have an estimated incidence of approximately 11 cases per year.

Whereas descriptions of esophageal atresia and tracheoesophageal fistulae date back to the 17th century, it was not until the end of the 19th century that the first attempt of surgical correction was undertaken by Steele. Furthermore, not until 1941 did Haight report the first successful repair for

this condition using a primary anastomosis. Since that time the success rate in the surgical treatment of these congenital defects has improved dramatically. In a historical review of 234 cases treated at the Royal Children Hospital in Melbourne, survival has improved from 31% during the period of 1948-1952, to approximately 90% in the latest decade from 1968 to 1977.<sup>2</sup> We became interested in documenting the results of the surgical treatment for this condition at the Ponce Regional Hospital, in order to identify any temporal changes in the outcome and to compare them with results at other institutions, locally and abroad.

### Materials and Methods

All cases with a diagnosis of esophageal atresia and/or tracheoesophageal fistula identified by the Record Room Division and from the Operating Room Records for the period of January 1969 to June 1981 were included. A total of 40 patients have been seen and treated at the Ponce Regional Hospital during this period. The initial 14 cases in the period from 1969 to 1973 have been previously reported by Torres Aybar et al.<sup>3</sup> The data from the remaining 26 cases, dating from June 1973 to June 1981, form the basis of this report. Complete records were available for 21 of these registered cases.

### Results

#### **Incidence, Sex Distribution and Clinical manifestations**

For the entire 12 year period, there were 40 cases, an incidence 3.3 cases per year. Of the 21 cases completely reviewed, 8 (38.1%) were born at the Ponce Regional Hospital, 11 (52.4%) were referred from other institutions, and 2 records (9.5%) did not document the place of birth. Eighteen (85.7%) were totally treated at the Ponce Regional Hospital, and 3 (14.3%) were referred to other institutions. Fifty three percent were females, 47% males. The most common presenting signs and symptoms were excessive salivation, vomiting and respiratory distress or pneumonia.

#### **Age at Diagnosis and Diagnostic Test (Tables I, II)**

Fifty two percent were diagnosed within the first 24 hours of life, 38% in 24 to 72 hours, and 9.5% more than 72 hours after birth. The passage of a nasogastric tube as a diagnostic test was attempted in 12 and this maneuver suggested esophageal atresia in all instances. All cases had a chest x-ray performed; in 86% of these the diagnosis was suggested. A contrast study was done in 18 of 21 patients and all were interpreted as diagnostic for esophageal atresia.

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*Reprint Request: Pedro J. Rosselló, M.D., Director, Surgical Research Laboratories, U.P.R. School of Medicine, G.P.O. Box 5067, San Juan, Puerto Rico 00936.*

TABLE I

Age At Diagnosis		
Age	Number	Percent
< 24 hrs.	11	52.4
24-72 hrs.	8	38.1
> 72 hrs.	2	9.5

TABLE II

Diagnostic Test		
	Performed	Diagnostic
Nasogastric Tube	12	12
Chest X-Ray	21	18 (86%)
Contrast Study	18	18 (100%)

**Types and Associated Anomalies** Tables III, IV, and Figure I)

Sixteen cases (76.2%) were type C (esophageal atresia with distal tracheoesophageal fistula); one case (4.8%) type B (esophageal atresia with proximal tracheoesophageal fistula); and four cases (19%) type A (esophageal atresia without fistula). We found no cases of types D or E (H-type) esophageal atresia. Other associated anomalies were present in 9 patients (42.8%). Most of these were cardiovascular (14.3%) or skeletal (19%). Low birth weight was present in 52.3%.

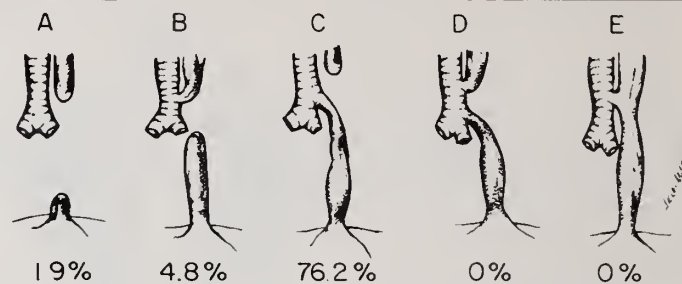
TABLE III

Type Distribution		
Type	Number	Percent
A	4	19.0
B	1	4.8
C	16	76.2
D	0	0
E	0	0
TOTAL	21	100

TABLE IV

Associated Anomalies		
	Number	Percent
I. Total Patient With Anomalies	9	42.8
A. Cardiovascular	3	14.3
B. Gastrointestinal	1	4.7
C. Downs Syndrome	2	9.5
D. Skeletal	4	19.0
II. Low Birth Weight	11	52.3%

Figure I



Types of esophageal atresia (after Gross) and the percentages of each found in the reviewed cases.

**Surgical Procedures** (Table V)

Primary repair of the esophageal atresia was the most common procedure utilized irrespective of the type of abnormality. In the most common type of esophageal atresia, that with a distal fistula, twelve of sixteen cases underwent a primary repair with division of the fistula and eight of these underwent simultaneous placement of a gastrostomy. Three cases were treated with division of esophageal fistula, cervical esophagostomy and gastrostomy, and one of these subsequently underwent a delayed colon interposition. One case underwent a gastrostomy alone and was referred elsewhere for further treatment. The one case of type B atresia, with proximal fistula, was also treated with division of the fistula and primary repair. It is interesting that three of four cases of type A atresia without tracheoesophageal fistula were treated with primary repair and gastrostomy. Only one of these required a cervical esophagostomy and gastrostomy as a preparation for a future esophageal reconstruction.

TABLE V

Surgical Procedures			
Procedure	A	Type	
		B	C
C.E. + G	1	-	-
P.R. + G	3	-	-
D.T.E. + C.E. + G			
LATE C.I.	-	-	2
D.T.E. + C.E. + G	-	-	1
G.	-	-	1
D.T.E. + P.R. + G	-	1	8
D.T.E. + P.R.	-	-	4
TOTAL	4	1	16

**Legend:**

C.E. - Cervical Esophagostomy  
C.I. - Colon Interposition

D.T.E. - Division Tracheoesophageal Fistula  
G. - Gastrostomy  
P.R. - Primary Repair



**Complications (Table VI)**

Most of the complications in these 21 cases were respiratory (11) or infectious (5), with sepsis occurring in 4 cases and a localized wound infection in one. Mechanical complications included stricture in four cases (Fig. 2), and anastomotic leak in one. Miscellaneous complications of post operative enteritis (3), anemia secondary to blood loss (3) and transient cardiac arrhythmias (2) also occurred.

**Figure II**

Anastomotic stricture, the most common mechanical complication in the reviewed cases.

**TABLE VI**

Complications	
Respiratory (Pneumonia/ Atelectasis)	11
Sepsis	4
Stricture	4
Enteritis	3
Anemia	3
Cardiac Arrhythmia	2
Anastomotic Leak	1
Wound Infection	1

**Survival (Table VII)**

Of 21 cases treated during the 1973 to 1981 period 14 survived (66.6%). This compares to a 16.6% survival between 1969 to 1971, and a 62.5% survival from 1971 to 1973. When we look at the relationship of birth weight to survival we find similar survival for those between 1.5 and 2.5 kilograms (63.6%) and for those between 2.5 and 3.5 kilograms (62.5%). Those above 3.5 kilograms had a 100% survival, although this group included only 2 cases.

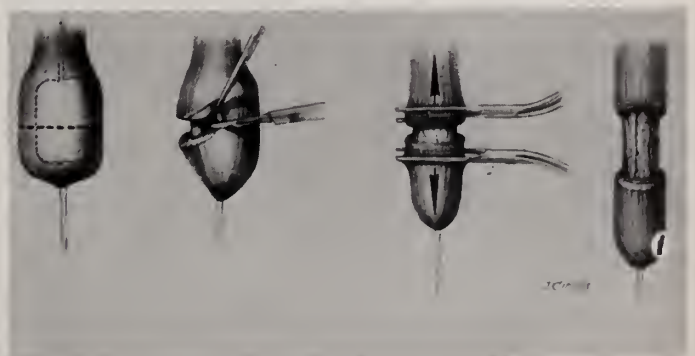
**TABLE VII**

Survival		
Period	Number Operated	Survived
1969-71	6	1 (16.6%)
1971-73	8	5 (62.5%)
1973-81	21	14 (66.6%)

**Discussion**

The clinical picture of esophageal atresia and tracheoesophageal fistula that emerges from our reviewed cases appears consonant with previous descriptions, with regards to demographic characteristics, clinical manifestations, diagnostic maneuvers and associated anomalies. The distribution of anatomic types follows the established pattern, except that we documented no type E cases (those with fistula without atresia). This may be due to the fact that these infants usually have their condition discovered at a later date, and may have been seen and treated at other institutions.

The surgical treatment included as the mainstay procedure a primary esophagoesophagostomy, performed in 10 of 21 cases. In three others the distance between the esophageal ends was too long for primary anastomosis and a palliative approach was used with the intent of completing a future esophageal reconstruction. This delay may be obviated

**Figure III**

The technique of esophagomyotomy for cases of long segment esophageal atresia

using recently described techniques to successfully approximate the esophageal segments in long gap esophageal atresia.<sup>4,5,6</sup>

Of greatest interest to us is the documented change in survival experienced by patients treated at the Ponce Regional Hospital. There has been a significant improvement in survival from 16.6% in the 1969-71 period to 66.6% in the latest period 1973-81. This parallels the historical experience at other institutions. Myers documented a marked rise in survival from 31% in the years 1948-52 to the 90% range in 1968-77.<sup>2,7</sup> Although the most recent experience at the Ponce Regional Hospital does not reach the excellent results at the Royal Children's Hospital, Melbourne, this may reflect the specialized nature of this latter institution with highly developed expertise in the management of diseases of children. Our results are not significantly different from those obtained at another institution in Puerto Rico,<sup>8</sup> and may in fact define the local state of the art level in dealing with this complex and difficult problem. A survey of the members of the surgical section of the American Academy of Pediatrics in the early 1960's revealed an overall survival of 61%,<sup>9</sup> not unlike our present status. This may imply that our local experience will improve during the present decade to achieve the level of excellent results now demonstrated possible.<sup>10</sup>

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## ¿QUE ES LA ASOCIACION MEDICA DE PUERTO RICO?

Es una asociación profesional voluntaria integrada por médicos. Se sostiene a través de las cuotas que pagan sus 2,500 socios. Tiene un personal administrativo no médico de alrededor de 17 personas.

Está dividida en seis Sociedades de Distrito, a saber: Este (con sede en San Juan), Sur (con sede en Ponce), Occidental (con sede en Mayagüez), Central (con sede en Caguas, Norte (con sede en Arecibo) y la Noreste, creada en 1982 con sede en Bayamón. Está afiliada además a la Asociación Médica Americana.

La Asociación persigue el mejorar la salud y el bienestar de todo el pueblo. A través de la prensa, radio, televisión y material impreso, trata de orientar al pueblo en lo referente a

un mejor cuidado de la salud. En cooperación tanto con las agencias gubernamentales como privadas, la Asociación vela por el bienestar de la comunidad, brindando su cooperación en campañas o actividades en beneficio de la salud de todo el pueblo. Impulsa o combate cualquier legislación estatal o federal si de acuerdo con sus principios ha de ser ésta favorable o nociva a la comunidad. Mantiene a los médicos informados de los programas científicos, a través de publicaciones, cursos post-graduados y seminarios, de manera que los pacientes se beneficien lo más pronto posible de los últimos descubrimientos aprobados.

A pesar de que la AMPR está constituida por médicos, la misma se creó para servir tanto al público como a la profesión. Sus múltiples actividades benefician a ambos.



# Los Patrones Mamográficos en Puerto Rico

Bernardo J. Marqués, M.D.

El cáncer de seno en Puerto Rico ocupa el primer lugar entre las malignidades de la mujer puertorriqueña si excluimos el cáncer *in situ* del cuello uterino. Es además la primera causa de muerte por malignidad en la mujer de nuestro país y la primera causa de muerte por cualquier motivo en las mujeres entre las edades de 40 y 49 años.<sup>1,2</sup> El diagnóstico temprano de cáncer de seno sigue siendo el único factor de impacto significativo y positivo en reducir la mortalidad y la morbilidad en esta enfermedad.<sup>3</sup>

Por muchos años, clínicos e investigadores han buscado con gran ahinco identificar factores que pudieran señalar al grupo de mujeres en riesgo mayor de desarrollar esta malignidad para así dirigir los mejores esfuerzos diagnósticos a ellas en busca de lesiones tempranas. Este factor o estos factores han probado ser altamente elusivos. Cuando los diez (10) factores clásicos con que tradicionalmente hemos determinado un riesgo aumentado en algunas mujeres tales como un historial familiar de cáncer de seno, nuliparidad, primer embarazo a término en edades avanzadas, y vida menstrual prolongada, fueron científicamente analizados, se encontró que solo el 21% de las mujeres entre los 30 y los 54 años con cáncer de seno tuvieron uno más de esos factores en su historial, y que solo 29% de aquellas sobre los 55 años y que padecieron cáncer de seno tenían uno o más de estos factores en el suyo.<sup>4</sup>

En el 1976 el Dr. John Wolfe, un radiólogo de Detroit, buscando igualmente ese elusivo factor de determinar un riesgo aumentado en algunas mujeres, publicó su primer artículo sobre patrones mamográficos.<sup>5</sup> En ese artículo el Dr. Wolfe categorizó la apariencia de los senos en mamografía (Fig. 1) y en base a su experiencia con más de 5,000 pacientes, determinó el riesgo relativo de cada uno de estos cuatro grupos. Los patrones N-1 y P-1 en la experiencia de Wolfe indicaban un bajo riesgo de desarrollar cancer de seno, mientras que los patrones P-2 y DY conllevaban un definitivo y sustancial riesgo mayor de desarrollar esta malignidad.

En sus inicios pareció muy prometedora esta clasificación de Wolfe y numerosos autores re-examinaron sus series a la luz de estos patrones para confirmar o refutar sus hallazgos y conclusiones. Surgieron y continúan surgiendo numerosos estudios en ambos bandos, es decir, unos confirmando y otros refutando la validez de los patrones de Wolfe

Figura 1

Patrones Mamográficos de Wolfe
N-1 Parenquima compuesta mayormente de grasa sin ductos visibles.
P-1 Ductos ocupando no más del 25% del seno.
P-2 Ductos prominentes ocupando sobre el 25% del seno.
DY Densidad displástica ocupa sobre el 10% del seno. Puede ocultar patrón P-2.
QDY Indeterminado. Mujeres más jóvenes.

como señaladores de riesgo. Radiólogos con un vastísima experiencia en mamografía como el Dr. Robert L. Egan<sup>6</sup> concluyeron en su análisis que el aumento en riesgo señalado por Wolfe para las mujeres con patrones mamográfico P-2 y DY era artefactual y que en realidad reflejaba únicamente una demora en el reconocimiento del cáncer presente en estas mujeres, debiéndose dicha demora al aumento en densidad de los senos en estos dos patrones dificultando la misma la identificación de la lesión maligna. Wolfe, y otros radiólogos insisten, sin embargo, en la validez de sus hallazgos.

Es de todos conocido que el cáncer de seno tiene una historia natural muy diferente en muchos de los países en los que ha sido estudiado tanto en su incidencia, como en su agresividad, edad de prevalencia y otros parámetros. Por esto entendimos que era deseable considerando estas diferencias, establecer la validez o la inutilidad de estos patrones mamográficos en las mujeres puertorriqueñas. Ciertamente, con las limitaciones de recursos en el país sería ideal poder identificar las mujeres en mayor riesgo de desarrollar cáncer de seno de alguna manera para concentrar los esfuerzos diagnósticos en estas.

Con esto en mente estudiamos dos poblaciones de mujeres sintomáticas pero sin cáncer de seno en el país. En nuestra experiencia sobre el 95% de las mujeres sometidas a mamografía en Puerto Rico son mujeres sintomáticas. (Fig. 2)

Figura 2

Dos Poblaciones de Mujeres Sintomáticas en P.R.
CMPR - 581 - reproducibilidad 90%+
PAVIA - 1208

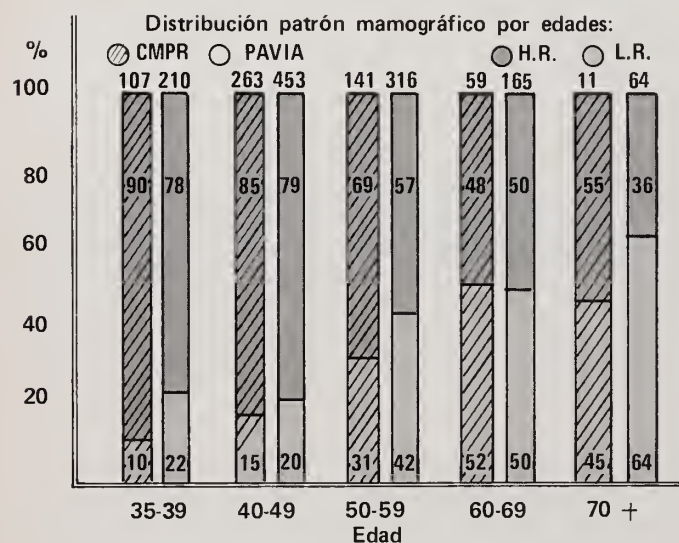
La población de 581 mujeres estudiadas en el Centro Médico de Puerto Rico es importante porque fue en este grupo que determinamos nuestra consistencia como observadores y adjudicadores de patrones mamográficos. En tres ocasiones diferentes estudiamos las mamografías de estas pacientes en manera "ciega doble" categorizando a las mismas en los 4 grupos de Wolfe. Nuestra coincidencia en la categorización por patrones mamográficos en este estudio excedió el 90%. Más importante aún varios Residentes de radiología que evaluaron estos casos al terminar su pasantía

de adiestramiento por nuestra División tuvieron una coincidencia de 88% o más con la apreciación nuestra, por lo que concluimos que la adjudicación de patrones tiene una gran reproducibilidad en nuestras manos y puede capacitarse a otros a tener una reproducibilidad comparable en un período de tiempo relativamente corto.

Debido a que en la población del Centro Médico de P.R. el número de pacientes sobre los 60 años es muy reducido, decidimos estudiar una población de 1208 pacientes sometidas a mamografía en el Hospital Pavía entendiendo que dicha población con una mejor distribución de edades y proveniente de una más amplia base de referido, era más representativa de la mujer sintomática en Puerto Rico. (Fig. 2)

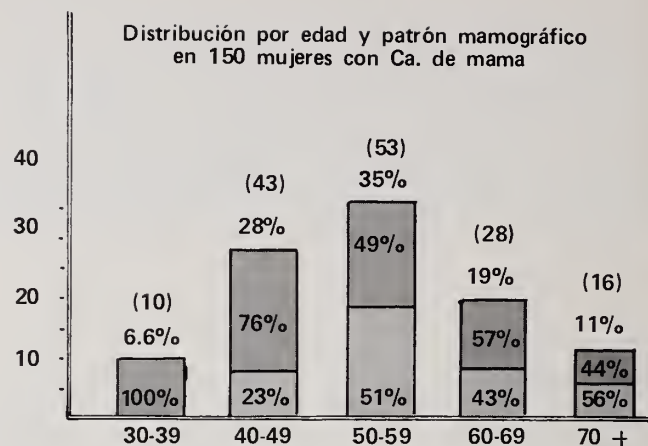
Al igual que otros autores agrupamos las pacientes con patrones N-1 y P-1 en la categoría de "bajo riesgo" (L.R. = low risk), y las pacientes con patrones P-2 y DY en la categoría de "alto riesgo" (H.R. = high risk). Observamos un paralelismo en la distribución de estas categorías mamográficas en cada sub-grupo de edades entre las mujeres estudiadas en el CMPR y las estudiadas en Pavía (Fig. 3) siendo la mayor diferencia entre estos grupos el número de pacientes envueltos en cada década estudiada. Observamos, como era de esperarse, que a mayor edad aumentan los patrones de "bajo riesgo" reduciéndose proporcionalmente los patrones de "alto riesgo" como consecuencia del remplazo del tejido mamario denso por tejido adiposo con el pasar de los años.

Figura 3



Estudiamos a continuación el patrón mamográfico en el seno opuesto en 150 mujeres con carcinoma de seno confirmado patológicamente en el CMPR analizando para propósitos comparativos las 140 de estas pacientes sobre los 40 años. (Fig. 4) Por debajo de los 40 años la densidad normal del seno es tal que no debe de adjudicarse un patrón mamográfico de las 140 mujeres con cáncer de seno sobre los 40 años de edad con los 1,208 pacientes sintomáticas pero sin cáncer de seno estudiadas en el Hospital Pavía. También sobre los 40 años de edad, notamos que la distribución de los patrones de "alto" y "bajo" riesgo en ambos grupos era

Figura 4



prácticamente idéntico en cada uno de los subgrupos por edades (Fig. 5), y al unir la totalidad de las pacientes con cáncer de seno sobre los 40 años y contrastarlas a la totalidad de las pacientes sintomáticas sin cáncer sobre 40 años, notamos que la distribución de patrones de "alto" y "bajo" riesgo en estos grupos era idéntica. (Fig. 6)

Figura 5

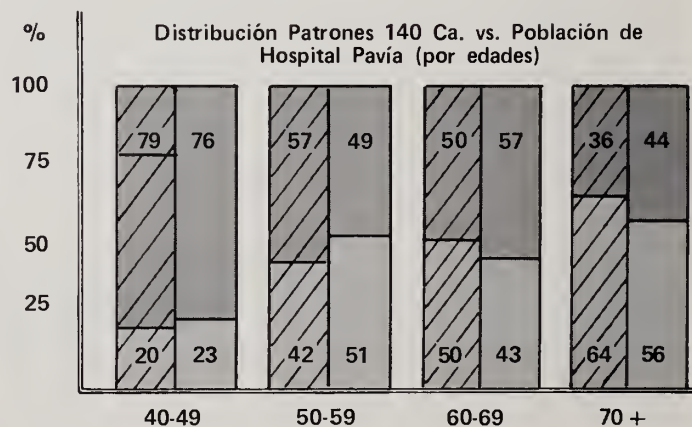
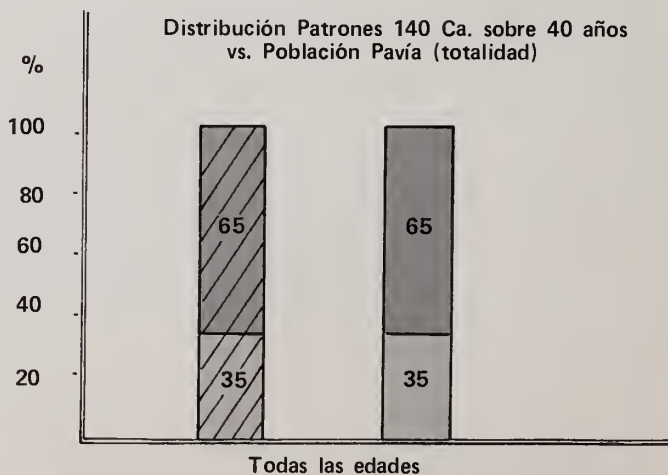


Figura 6





### Conclusión

En vista de esto concluimos que en nuestra experiencia en Puerto Rico, el patrón mamográfico en las mujeres sintomáticas sobre los 40 años de edad, no tiene utilidad alguna en el señalamiento de un riesgo real en estas pacientes y que la única utilidad de los patrones mamográficos más allá de su función descriptiva es la de alertar tanto al Radiólogo como al clínico que en mujeres categorizadas mamográficamente como P-2 o DY, dada la densidad significativamente mayor de estos senos, podría demorarse un diagnóstico de carcinoma al estar este oculto por un período mayor entre los tejidos densos de estos senos. Nos parece, por tanto, que los clínicos deberán considerar a toda mujer mayor de 35 o 40 años como una en riesgo sustancial de desarrollar cáncer de mama irrespectivo del patrón mamográfico de sus senos.

**Resumen:** El patrón mamográfico en 140 mujeres de 40 años o más con cáncer de seno fue analizado y contrastado con un grupo control de 1,208 mujeres de igual edad sintomáticas pero sin evidencia de cáncer de seno. La distribución de los patrones de "alto" y "bajo" riesgo en ambos grupos fue idéntica. Por tanto concluimos que en nuestra experiencia en Puerto Rico no es la clasificación o identificación de mujeres en mayor o menor riesgo de desarrollar cáncer de seno por el patrón mamográfico de "alto" o "bajo" riesgo de las mismas.

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## SIRVIENDO AL PUEBLO Y A LA PROFESION MEDICA



ASOCIACION MEDICA DE PUERTO RICO

# Rehabilitation of Patients With Bone Tumors Treated by Various Methods Including Cryosurgery\*

W. Russe, M.D.  
R. Siorpaes, M.D.

**Abstract:** Bone tumors taken as a whole are a relatively frequent disease. But when we differentiate the individual tumors—benign, malignant, primary, secondary—the subgroups concern very different numbers of patients. The treatment of the patients, namely their rehabilitation, has completely different aims and therefore also different techniques are applied. We got down to these problems on the basis of the case material of our hospital between 1972 and 1981. Our technique of cryosurgery is introduced in short.

During the past ten years, from 1972 to 1981, 272 benign bone tumors and tumor-like bone lesions, 87 primary and 227 secondary malignant bone tumors were treated at our department.

First the most frequent group of tumors, the secondary malignant tumors or metastases. In these cases the task of the orthopedic surgeon is to treat impending fractures or pathological fractures already occurred. There can usually nothing be done as to the fate of such patients in regard to the basic disease, but if there are pathological fractures surgery can certainly make the often but few remaining months worth living or make care of these patients easier. In the extremities either a composite internal fixation or an endoprosthetic bone or joint replacement is performed; the choice of the operative procedure depends on the location and the size of the tumor.

For bone metastases 44 composite internal fixations and 58 endoprosthetic replacements in extremities were performed during the past ten years. While the composite internal fixation is most frequently indicated in the diaphyses, the endoprosthetic replacement has shown excellent results in the hip joint. Less satisfactory is the replacement of the knee joint and the proximal humerus.

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\* Paper presented at the 4th Congress of the International Rehabilitation Medicine Association (IRMA), San Juan, Puerto Rico, April 1982.

(Case 1, 2) In the hip we use the *Mathys-Müller* tumor-prosthesis, in the knee joint various types of prostheses. In the shoulder *Mathys* is used. (Case 3, 4, 5). All these prostheses are available in some standard sizes and custom-made for larger resections. Two very seldom indications for endoprosthetic replacements are pelvic lesions and the replacement of total bones. (Cases 6, 7).

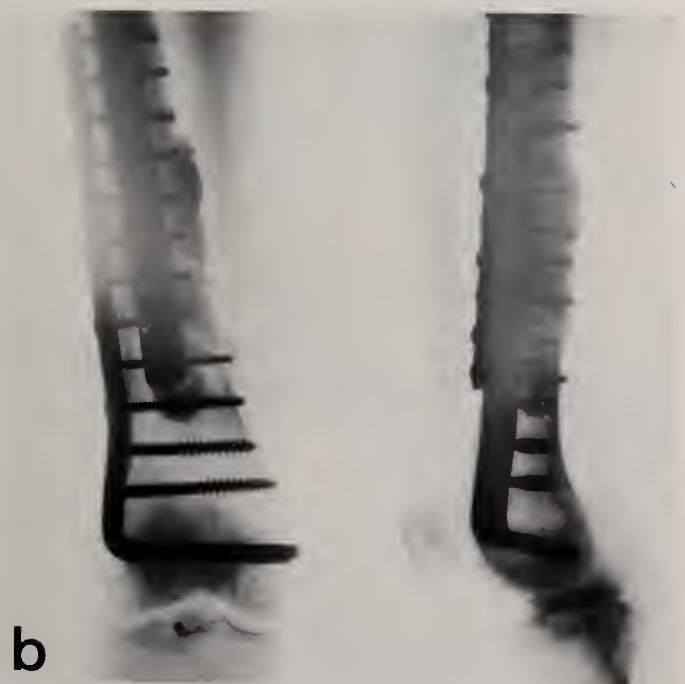


Case 1. B.J., female, 68 years old, lung cancer, imminent spontaneous fracture right proximal humerus. Treatment by composite internal fixation.  
a) radiographs preoperative b) radiographs 3 weeks after operation.





Case 3: S.L., female, 47 years old, breast cancer, solitary metastasis left proximal femur. Treatment by wide local excision and endoprosthetic replacement by a Mathys-Müller tumor endoprosthesis.  
a) radiograph preoperative b) radiograph 1 year after operation.



Case 2: V.R., male, 58 years old, lung cancer, spontaneous fracture right distal femur. Treatment by composite internal fixation.  
a) radiographs preoperative b) radiographs 3 weeks after operation.

Case 4: H.A., female, 53 years old, malignant fibrous histiocytoma. Treatment by wide local excision and endoprosthetic replacement by a modified GSB tumor endoprosthesis.  
a) radiographs preoperative b) radiographs 3 months after operation.



Case 5: F.A., female, 27 years old, malignant giant-cell tumor. Treatment by wide local excision and endoprosthetic replacement by an isoelectric humerus prosthesis after *Mathys*  
a) radiograph preoperative b) radiograph 3 years postoperative.



Case 6a: K.F., female, 40 years old, breast cancer, metastasis and spontaneous fracture of the right acetabulum. Treatment by marginal excision and custom prosthetic replacement. Radiograph Preoperative.



Case 6b: Pattern built by the computerized axial tomograms and custom made prosthesis.



C

Case Case 6c: Radiograph 2 years after operation.



Case 7: S.F., female, 70 years old, breast cancer, solitary metastasis and several spontaneous fractures of the whole left femur. Treatment by marginal resection and total-femur prosthetic replacement.

a) radiograph preoperative b) radiograph 6 months after operation.

The vertebral column is usually stabilized by composite internal fixation. When operating from the back the Harrington instrumentations is used, from ventral we use various plates, such as the *Orozco*-plate in the cervical spine and various AO-plates in the other parts of the vertebral column. Vertebral bodies can be replaced by *Polster*-prostheses. (Cases 8, 9, 10).



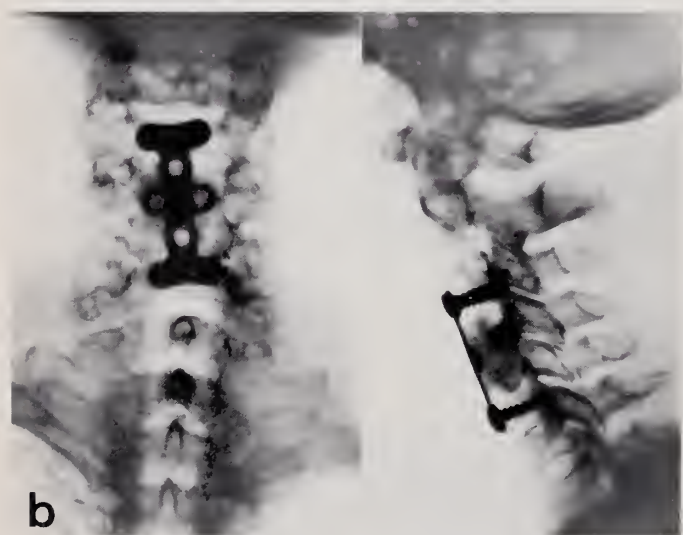
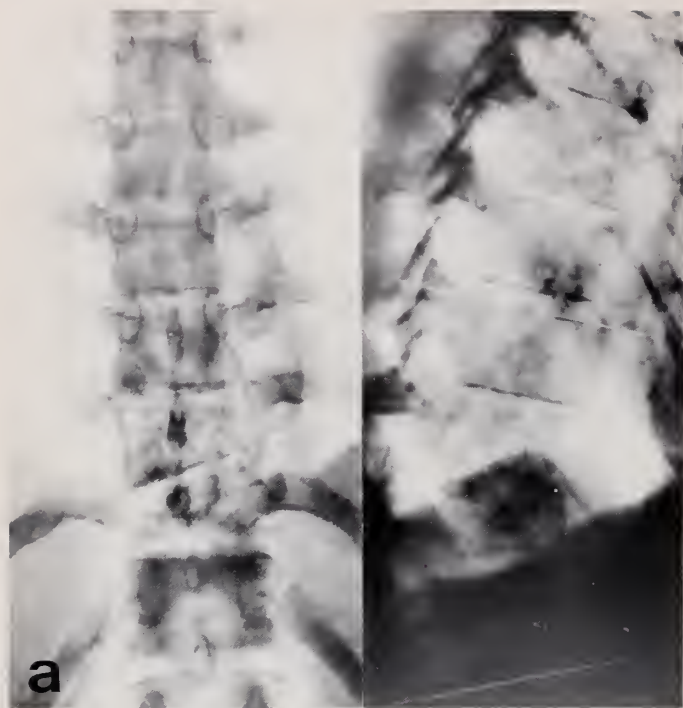
Case 8: T.R., female, 33 years old, carcinoma of the uterus, multiple bone metastases, compression syndrome of the spine. Treatment by decompression and stabilization by composite internal fixation with *Harrington* rods.

a) radiograph preoperative b) radiograph 1 month after operation.



Case 9: H.H., male, 42 years old, plasmacytoma, osteolysis of the 4th cervical vertebral body, beginning compression syndrome of the spine. Treatment by ventral decompression and stabilization by composite internal fixation with the *Orozco* plate.

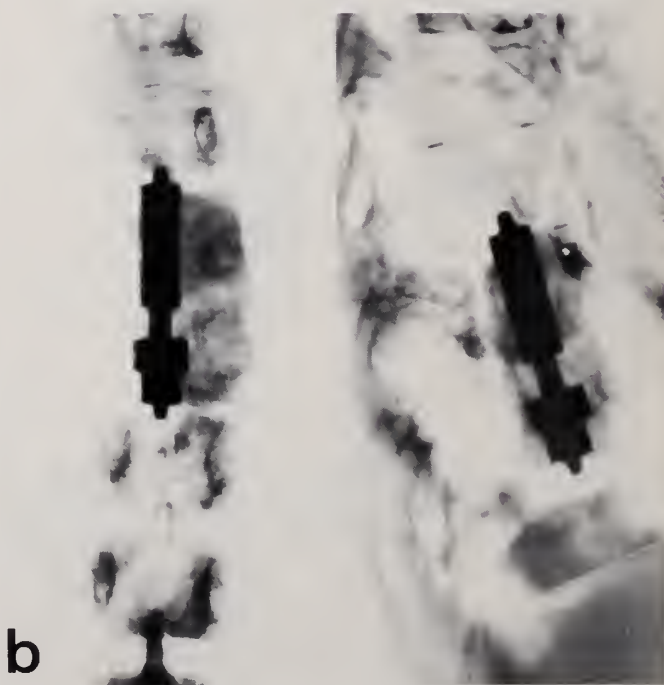
a) radiographs preoperative b) radiographs 6 months after operation.



Case 10: G.K., female, 37 years old, breast cancer, multiple bone metastases, osteolyses of the 11th and 12th thoracic vertebral bodies, beginning compression syndrome of the spine. Treatment by ventral decompression, marginal excision of the vertebral bodies and prosthetic replacement by the *Polster*-prosthesis, additional bone cement.

a) radiograph preoperative b) radiograph 6 months after operation.

Concerning the primary bone tumors, we should first like to talk about the benign and semi-malignant bone tumors and the tumor-like bone-lesions. As the frequency of recurrences of such kind of tumors ranges from 0 to 70%, we introduced additional measures for the local devitalization of the tumor, especially for semi-malignant tumors, for which some authors advocate en-bloc resection. After three years of basic research and experiments on animals, cryosurgery, which was introduced in Orthopedics by *Marcove* many years ago, was further developed at our

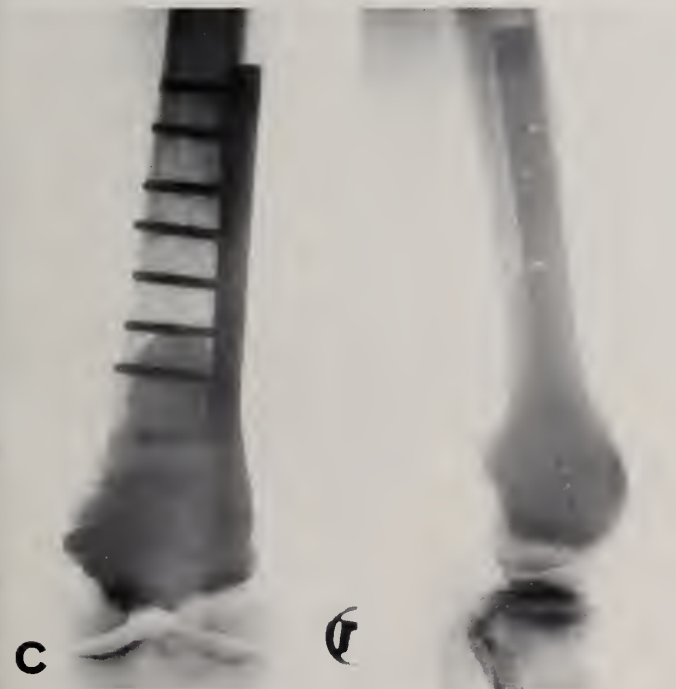


Case 11a: P.H., male, 29 years old, giant-cell tumor, pathologic fracture left distal femur. Treatment by curettage, cryosurgery and composite internal fixation.





Case 11b: Freezing of the cavity by a bullet probe.



Case 11c: Radiographs after operation.

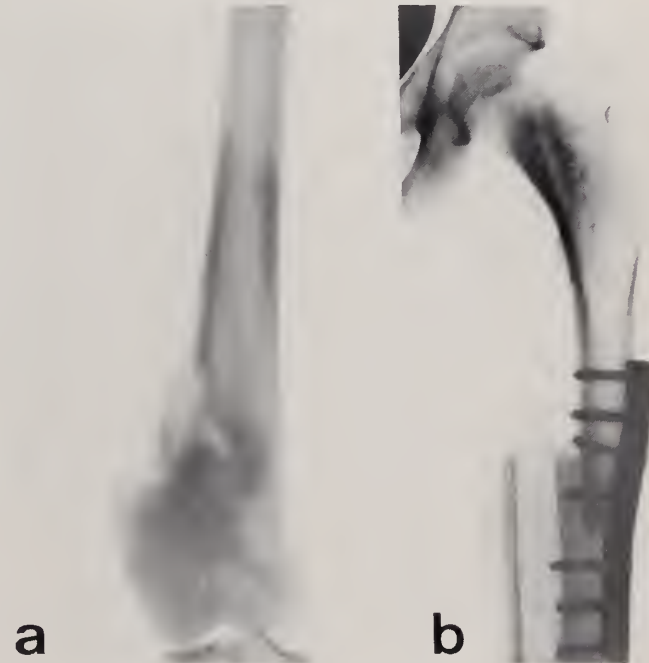
hospital and has by now been clinically applied for three years. Sixty patients were treated by cryosurgery till now. It would certainly be too early to state final results, but we should like to present the method by means of one case. (Case 11).

In most cases after curettage and cryosurgery the cavity is bridged by various bone grafts, smaller defects are usually filled with autologous bone grafts.

Much more difficult is the treatment of primary malignant tumors, as more than 50% of the cases occur during childhood. The most frequent tumors are the osteogenic sarcoma and Ewing's sarcoma. The application of new chemotherapy-schemes could significantly improve the prognosis for such patients. This must also be considered when planning the operation.

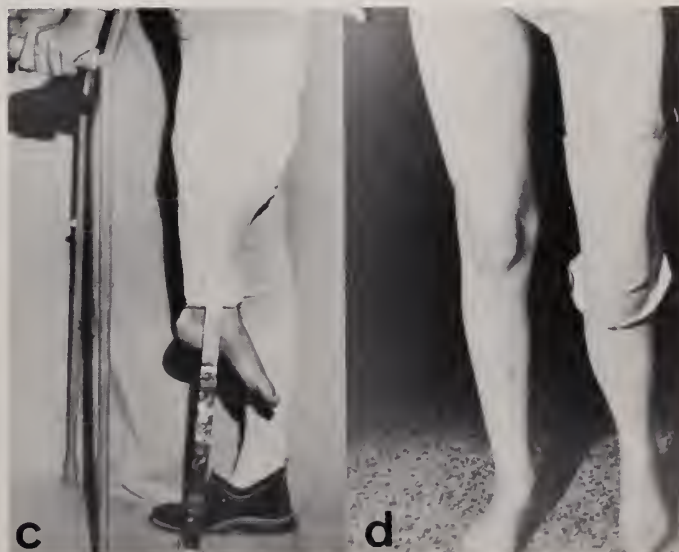
In former times, certainly also because of the bigger size of the tumors, the amputation was the treatment of choice, especially with osteogenic sarcoma. Today in an increasing number of select cases resections are carried out. On these patients special operative techniques must be applied because of the many problems of endoprosthetic replacements and because the skeleton is often still in growth. Beside several resection-arthrodeses performed at our

hospital we also perform rotationplasty after *Borggreve* for tumors in the distal femur which is the most frequent location for those tumors. After the resection of the knee joint the remaining part of the leg is rotated 180 degrees and fixed to the femur by internal fixation. Depending on the age of the patient, the resection must be planned in a way that after the completion of growth the axis of the ankle joint of the operated leg is finally at the same level as the knee joint of the other leg, so that the ankle joint can take over the function of the knee joint. Although this operation causes cosmetic problems in the beginning it shows excellent functional results. In contrast to an above-knee amputee these patients have their own active mobility of a knee joint. They are free of phantom limb pain and stump problems because they have their own weight-bearing foot. (Case 12).



Case 12: J.B., female, 13 years old, osteogenic sarcoma left distal femur. Treatment after preoperative chemotherapy by wide local excision and rotationplasty after *Borggreve*.

a) preoperative radiograph b) radiograph 2 weeks after operation



Case 12 c & d Patient 2 weeks after operation weeks after operation. Patient with the final prosthesis.

In Ewing's sarcoma, because of the high number of secondary malignant tumors deriving from a combined application of radiotherapy and chemotherapy, the surgical approach is also increasingly given preference.

### Conclusion

We can say that the past ten years have brought about a significant change in regard to both the operative treatment and the conservative therapy like radiation and chemotherapy. We must continue to keep an eye on current studies and recordings and evaluate them critically. The various therapeutic measures must be elaborated and applied in cooperation with other disciplines.

Altogether it must be our aim to achieve a maximum possible functional result by the minimum possible operation to procure the best possible rehabilitation for the patient-regarding oncological principles at the same time.

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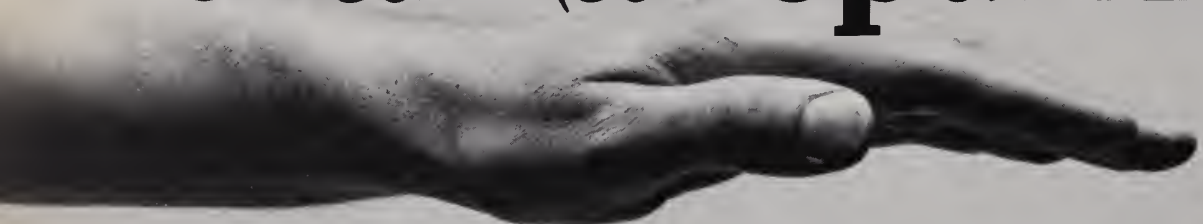
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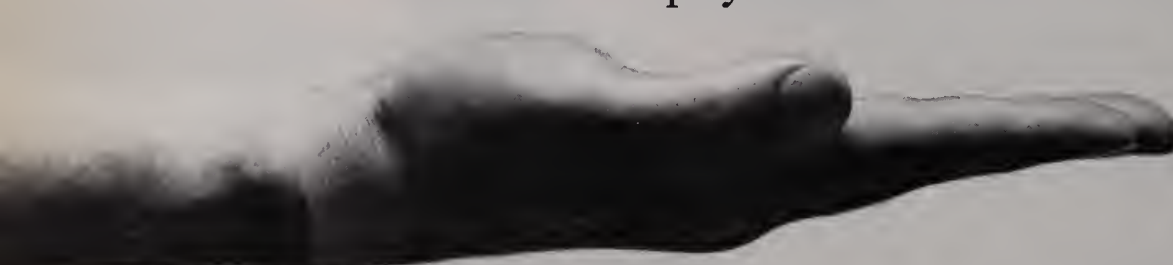
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# Presentación de Casos

## Beneficial Effect of Captopril in a Patient with Congestive Heart Failure and Ischemic Interventricular Septal Rupture

Guillermo Cintrón, M.D.  
José R. Rivera del Río, M.D.  
Juan M. Aranda, M.D.  
Edgardo Hernández-López, M.D.  
Esteban Linares, M.D.  
Eli A. Ramírez, M.D.

Ventricular septal rupture is one of the most dreaded complications of acute myocardial infarction having an early mortality of 65% and almost 90% at two months<sup>1</sup>. With the use of hemodynamic monitoring, vasodilators and new inotropic agents, it has been possible to obtain better control of the early cardiac decompensation commonly seen in these patients and thus decrease the risks associated with early emergency surgical intervention.

Recent studies in patients with congestive heart failure have shown the the renin-angiotensin-aldosterone system plays an important part in its pathophysiology.<sup>2</sup> The renin-angiotensin-aldosterone system is activated by the decreased cardiac output and renal perfusion present in patients with severe heart failure. These findings have led to the use of the angiotensin I converting enzyme inhibitor Captopril in patients with congestive heart failure. The acute and long-term use of this drug has been demonstrated to produce a decrease in pulmonary wedge pressure, increase in cardiac output and improvement in functional status in these patients.<sup>3,4</sup>

The use of captopril in patients with ruptured interventricular septum has not been reported previously. We report the use of captopril in a patient with ventricular septal rupture due to acute myocardial infarction complicated with severe cardiac failure.

### Case Report

The patient, a 51-year-old male with a history of high blood pressure, developed an acute anterolateral myocardial infarction on May 7, 1981. While hospitalized he developed

signs and symptoms of congestive heart failure and was treated with diuretics and oral nitrates. Digoxin was added after discharge at an outpatient visit because of the persistence of heart failure symptoms. On June 18, 1981 the patient was again admitted to the hospital with symptoms of progressive heart failure. Administration of sodium nitroprusside controlled the symptomatology transiently; three days later there was further clinical deterioration and a harsh, loud, holosystolic murmur was first heard. Echocardiographic studies were compatible with a ruptured interventricular septum and the patient was transferred to our institution. Upon admission to our hospital the patient's blood pressure was 110/70 mm Hg; heart rate 134 per minute. Grade II hypertensive retinopathy was present. Cardiovascular examination demonstrated bibasilar rales, left ventricular impulse at the sixth intercostal space at the left anterior axillary line, a grade 3/VI holosystolic murmur over the whole precordium and S3 and S4 gallops. The EKG showed left ventricular hypertrophy, left atrial enlargement, left anterior hemiblock and evidence of anterolateral transmural myocardial infarction with persistent S-T elevation. The presence of the ruptured interventricular septum with a 2:1 pulmonary-to-systemic flow ratio was documented by Swan Ganz right heart catheterization. The patient was treated with digoxin, diuretics and parenteral vasodilator (sodium nitroprusside) with a satisfactory hemodynamic response as demonstrated by a diminution of the pulmonary wedge pressure from 22 to 10 mm Hg. Oral vasodilators (isosorbide dinitrate and hydralazine) were then started and the parenteral vasodilator was discontinued. Within one week the patient's condition deteriorated and the parenteral vasodilator had to be restarted. The patient again improved and the parenteral vasodilator was substituted by oral medication. Signs of progressive cardiac decompensation appeared again and the oral vasodilators were then substituted by the converting enzyme inhibitor Captopril. With this substitution the patient's condition stabilized and eventually improved from functional class IV to class III. Measurements of urinary sodium excretion and fractional sodium excretion showed a progressive natriuresis and the blood urea nitrogen gradually decreased after the institution of captopril therapy (Figure 1). Radionuclide ventriculography and coronary cineangiography demonstrated a left ventricular ejection fraction of 15%, a large anterior akinetic area and severe proximal disease of the left anterior descending coronary artery. One month after admission, the patient underwent successful aneurysmectomy and repair of the interventricular septal rupture. The patient was discharged after an uncomplicated post-operative course on digoxin 0.25 mg daily and chlorthalidone 50 mg daily in a functional class II status.

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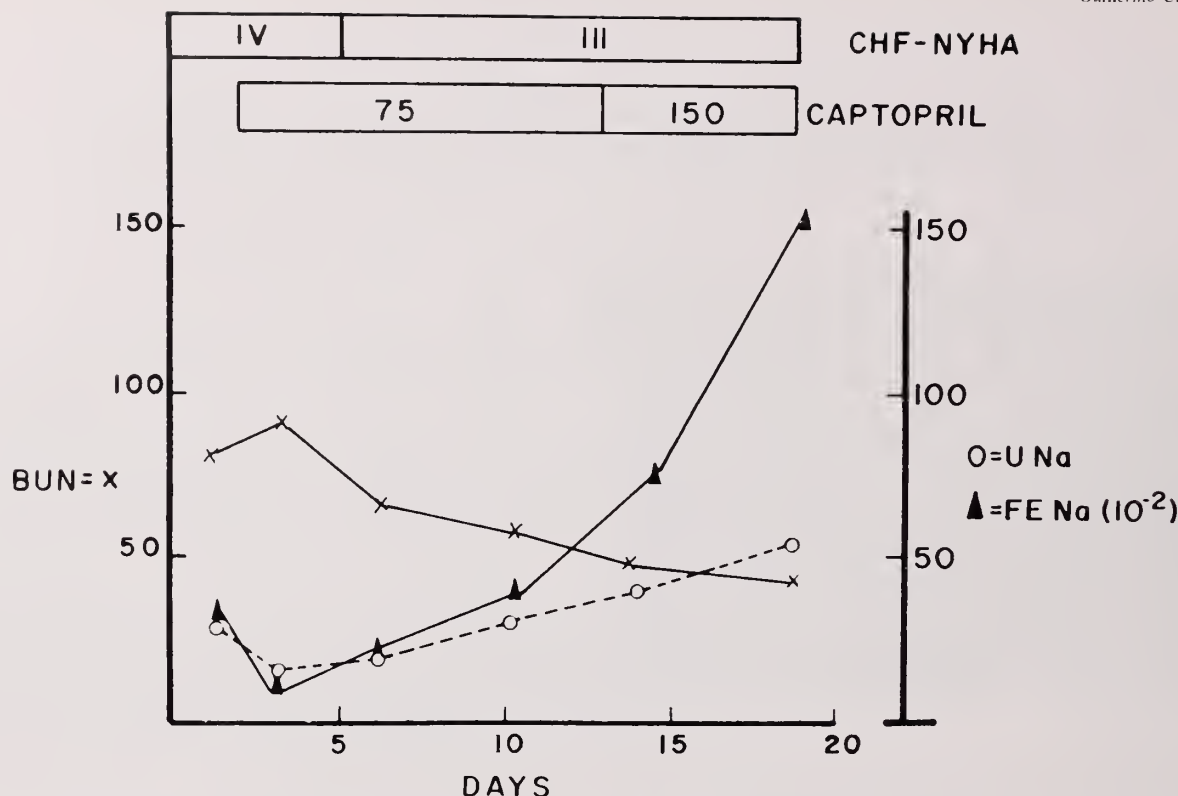


Figure 1. Natriuretic response to Captopril in a patient with severe heart failure due to ischemic interventricular septal rupture. Drug therapy in milligrams per day.

CHF-NYHA: Congestive heart failure symptoms as classified by the New York Heart Association.

U Na: Urinary sodium excretion in milliequivalents per liter.

BUN: Blood urea nitrogen in milligrams per deciliter.

FE Na: Fractional sodium excretion.

### Discussion

Present day pharmacologic therapy for patients with severe congestive heart failure is based on the use of digitalis, diuretics and vasodilator drugs. Dzau et al<sup>5</sup> have shown that patients who are unresponsive to this therapeutic regime may improve further by the substitution of vasodilator drugs with converting-enzyme inhibitors.

Vasodilator drugs will produce beneficial effects in animals with experimental ventricular septal defect and have been recommended in this setting by some investigators.<sup>6,7</sup> In our patient the use of nitroprusside was unsuccessful in controlling symptoms and clinical deterioration ensued. The response of our patient to converting enzyme inhibitor was similar to the response seen in patients with severe congestive heart failure treated in similar fashion by other investigators.<sup>4,5</sup>

The response of this patient to Captopril suggests that this drug may be of particular value in the medical therapy of patients with ventricular septal defect and severe congestive heart failure. Such therapy may stabilize the patient until the time that corrective surgery can be accomplished with a reasonable chance of success.

**Resumen:** En este reporte presentamos el caso de un paciente con rotura de septo interventricular y fallo cardíaco tratado con Captopril.

Un paciente, un varón de 51 años de edad y con historial de

hipertensión arterial, sufre un infarto de miocardio con síntomas tarde aparece un soplo holosistólico. La presencia de rotura del septo interventricular se documenta por cateterismo cardíaco derecho y ecocardiografía y se trata su fallo cardíaco con digoxin, diuréticos y nitroprusiato de sodio. Se intentó dos veces en éxito, de sustituir el nitroprusiato con isordil e hidralazina. Cuando se sustituye nitroprusiato con Captopril, se consigue control de los síntomas de fallo y se documenta una natriuresis y disminución de la azotemia. Un mes más tarde el paciente es operado, se le repara la rotura del septo y es dado de alta.

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# ARTICULOS ESPECIALES

## Perspectivas Futuras Para el Diabético y sus Familiares

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El tratamiento del diabético desde el advenimiento de la insulina con Banting y Best ha sido el mismo, variando tan solo la pureza de la misma y las técnicas de inyección. En los años pasados todo se ha centrado en la insulina en sí, lo mismo habrá de ocurrir con los proyectos actuales y futuros. Los avances de la Ingeniería Genética ya permiten su síntesis inducida en bacterias, y en un futuro, con toda probabilidad, permitirán la inducción de su síntesis por células que por alguna razón han dejado previamente de producirla. Por ello consideramos halagador el futuro del diabético.

Los avances tecnológicos han permitido el desarrollo de múltiples instrumentos que ayudan a una dosificación de la glucosa más exacta, más práctica, y con menores inconvenientes al paciente. Técnicas de micrométodos, a su vez permiten la administración más exacta y más cuidadosa de la insulina. Además tenemos dosificadores de glicemia como el Glucometer, Dextrometer, Glucocheck, Reflomat, Rapid Gluco Test, el "páncreas artificial" de la Cia. Ames, y múltiples sistemas de inyección programada o continua desarrollados en Europa, Japón y Norteamérica. Al presente estos instrumentos permiten un mejor control del sujeto que, se espera habrá de disminuir las complicaciones crónicas de la enfermedad.

Por su interés, discutiremos ampliamente los avances en genética y sus implicaciones para el campo de la diabetología del presente y del futuro.

### Avances en Genética y Diabetes

En la última década las aplicaciones de la moderna Genética Médica al campo de la diabetología han sido de

importancia extraordinaria, destacándose fundamentalmente los experimentos en inmunogenética, la genética bioquímica y la ingeniería genética. Con toda probabilidad la terapia futura del diabético, al igual que el diagnóstico y el pronóstico, vendrán guiados por conceptos y técnicas de esta ciencia.

### I. Marcadores Genéticos

La Diabetes Mellitus es una condición heterogénea en cuya etiopatogenia influyen tanto factores hereditarios como ambientales.<sup>1</sup> La identificación de marcadores genéticos asociados o relacionados con la condición permitirá dilucidar más claramente su etiopatogenia. Al presente se evalúan varios marcadores (figura 1) y con toda probabilidad en los próximos años la lista se alargará extensamente.

Figura 1

Marcadores Genéticos
— HLA B8, B15, B18 Cw3, DRw3, DRw4 A2
— Efecto Antabus Clorpropamida
— C4F <sub>s</sub> <sup>o</sup> , C4f <sup>o</sup> S
— IF Membrana Muscular Extracelular
— Factor Kidd
— Polimorfismo Cromosoma 11

Estudios inmunogenéticos tienden a mostrar la prevalencia de ciertos antígenos de histocompatibilidad en los diabéticos insulínodpendientes (tipo I) y sus familiares inmediatos. Estos antígenos de histocompatibilidad pueden variar según el origen étnico de la población. Los genes responsables de dichos antígenos estarían localizados en los brazos cortos del cromosoma 6 a nivel de varios "loci". Los del locus D parecen estar asociados a trastornos inmunológicos.

Los antígenos de histocompatibilidad (HLA) que se han

descrito con mayor frecuencia entre diabéticos insulino-dependientes respecto a la población en general son: HLA-B8, HLA-B15, Cw3, DRw4, B18, A2. Los antígenos HLA-B y DRw2 estarían asociados en un menor riesgo de la condición por lo que algunos autores les han llamado "factores protectores", aunque ello parece reflejar un desequilibrio de ligamiento.<sup>2</sup>

Los antígenos HLA-B8 y B-15 varían en su incidencia con la edad del comienzo de la diabetes, sugiriendo, una vez más, la heterogeneidad de la condición (figura 2), los HLA-B8 se encontrarán con más frecuencia en los diabéticos jóvenes, a la vez que en todas las edades descritas en la figura 2. Los HLA-B15 son más frecuentes en los diabéticos que en la población en general, comparados con los B-8, lo que los convierte en un factor de mayor riesgo, al igual que los Dw3.

Figura 2

Frecuencia HLA-B8 y B-15 y Edad Inicio Diabetes		
Edad Comienzo (Años)	Porcentaje	
	HLA-B8	HLA-B15
0-5	44	0
6-10	48	23
11-15	56	8
16-20	28	17
21-25	37	21
26-30	47	18
Todos	49	21
Controles	31	10
Riesgo Relativo	2.17	2.35
Riesgo Relativo ambos	4.65	
Más de 31 años	37	10
Según Soeldner, J. <sup>4</sup>		

Aquellas personas que tienen haplotipo DR3 o DR4 tienen un riesgo 3 - 4 veces mayor que la población general de desarrollar diabetes insulino-dependiente. Aquellos que tienen ambos presentan un riesgo de hasta 20-40 veces, como se ha observado en algunas poblaciones Caucásicas.<sup>2</sup>

El agrupamiento de ciertos grupos HLA ha sido observado por Cudworth y otros<sup>4</sup> en ciertas familias de diabéticos. Se ha observado la presencia de dos tipos de asociaciones —tipo 1: A1B8(Cw4)-Dw3/DRw3; tipo 2: A2B15-Cw3-Dw4/DRw4. La presencia de estos grupos en un sujeto no afectado, familiar de un diabético, permitió a Cudworth y su grupo seguir la evolución de la condición en un sujeto hasta que presentó la diabetes manifiesta.

La incidencia y la severidad de la retinopatía es mayor en sujetos con grupos HLA específicos, como ha sido observado por el grupo de Cudworth, encontrando que la presencia combinada de DRw4-Dw4-B15Cw3A2 conlleva un riesgo de retinopatía de 3 - 4 veces.<sup>4</sup>

Tres combinaciones de haplotipos distintos son más frecuentes en diabetes que aparece a distintas edades. Así, a la edad de 10 o menos años: HLA 18-BfF1-DR3-C4x; a los 20 años o más: HLA-B15-C2<sup>2</sup> - Bf<sup>5</sup> - C4M - DR4; y a cualquier edad: HLA b8 -C2<sup>1</sup> - Bf<sup>5</sup> - C4F<sup>0</sup> - DR3.<sup>2</sup>

La deficiencia parcial o total del complemento C4 parece estar asociada con un mayor riesgo de diabetes en la población vasca francesa. El haplotipo C4F<sup>0</sup> no permite la expresión de C4S<sup>0</sup> y puede ser considerado como el responsable de una deficiencia parcial de C4, como ocurre también con otro haplotipo de C4, el C4 F<sup>0</sup>S. Este último suele encontrarse asociado con HLA-B8 y el C4F<sup>0</sup> con el HLA-B15. El complemento C4 ejerce una función importante en la neutralización de virus y su deficiencia podría favorecer a la acción de los virus diabetogénicos en las poblaciones susceptibles.<sup>4</sup>

En años recientes, diversos investigadores han revivido el conocido efecto antabús de la sulfonilurea clorpropamida, la cual, en determinados sujetos induce, tras la ingesta de alcohol, enrojecimiento de la cara y otras áreas corpóreas en ciertos diabéticos. Dicho efecto es más frecuente en los diabéticos no-insulino-dependientes (tipo 2), pero no es exclusivo de estos ya que se pueden observar en un número significativo de pacientes tipo 1 y sus familiares no diabéticos. El carácter inicial de marcador genéticos importante ha disminuido al observarse en ambos tipos de diabéticos. Sin embargo, puede aun ser útil para el estudio de ciertas familias y sus posibles relaciones con las complicaciones.<sup>2-3</sup>

Parece ser que este efecto antabús corre en familias en forma dominante, estando íntimamente ligado a los genes diabetogénicos. El enrojecimiento del efecto antabús de la clorpropamida puede ser inducido y reproducido en sujetos susceptibles con una infusión de un análogo de la met-enkefalina, y bloqueado por Naloxone. Este efecto antabús puede ser inhibido por Naloxone y por aspirina, al inhibir estos a nivel periférico las prostaglandinas circulantes.

Los sujetos con efecto antabús a clorpropamida positivo suelen presentar menor incidencia de retinopatía diabética, a la vez que presentan menor temperatura facial basal. Esto podría deberse a una vasoconstricción local, que a su vez poría ser el factor principal asociado con la menor incidencia de retinopatía.

El efecto antabús de clorpropamida puede ser impedido, en la mayor parte de las veces, por aspirina,<sup>9</sup> pero no ocurre así con la indometacina<sup>10</sup> Existen dos grupos diferentes, los que responden y los que no responden a la inhibición con indometacina. Estos últimos suelen ser los que presentan enfermedad micro, o macrovascular severa, los diabéticos no-insulino-dependientes suelen tener mayor positividad al efecto antabús. A su vez, los diabéticos no-insulino-dependientes, tienen una incidencia de complicaciones vasculares menor que los insulino-dependientes. Los diabéticos no-insulino-dependientes, en los cuales el efecto antabús es impedido por la indometacina, parecen estar protegidos de las complicaciones vasculares. Como la indometacina es un inhibidor de la síntesis de prostaglandinas, ello sugiere que estas pueden estar envueltas en la patogenia y la severidad de las complicaciones vasculares.

Barbosa y colaboradores<sup>11</sup> han encontrado una mayor incidencia de inmunofluorescencia para albúmina e IgG en la membrana extracelular muscular de sujetos no diabéticos con HLA idéntico al de sus hermanos diabéticos insulino-dependientes. En dichos sujetos no se observan anomalías metabólicas evidentes de diabetes, incluyendo estudio de glicemia y de hemoglobina A<sub>1</sub> C, lo cual sugiere que las anomalías inmunohistoquímicas observadas en las membranas extracelulares podrían no ser secundarias a la hiperglicemia y ser debidas a alteraciones tisulares genéticas.

Estudios realizados en los últimos dos años tienden a implicar genes diabetogénicos o sus modificadores localiza-



dos en más de un cromosoma. Así se han localizado en el cromosoma 2 los genes determinantes del factor Kidd,<sup>12</sup> en el cromosoma 6 los determinantes de los haplotipos HLA, y en el cromosoma 11, Nerup ha identificado un polimorfismo en familiares de diabéticos no-insulinodependientes que no están afectados por la condición<sup>13</sup>, que se transmite en forma dominante, y que constituye el primer marcador asociado a los cromosomas y el DNA descrito para los diabéticos no-insulinodependientes. En este mismo cromosoma esta localizado el gen responsable de la producción de insulina en el ser humano. Con toda probabilidad en un futuro no muy lejano se identifiquen otros marcadores en éstos y otros cromosomas, permitiendo en un futuro mapas genéticos específicos para cada familia que contribuirán a identificar los sujetos a riesgo, identificar la asociación con complicaciones, y quien sabe si llevarán a lo que hoy consideramos utopía: la reparación genética.

Todos estos hallazgos nos llevarán, en un futuro, a la responsabilidad ética de evaluar a los diabéticos con estas pruebas para determinar su posible "genotipo familiar", el cual podría estar asociado a los genes diabetogénicos. De forma responsable habría de realizarse un Asesoramiento Genético adecuado con la identificación de los familiares y sujetos a riesgo (figura 3). En países como los Estados Unidos de Norteamérica, donde abundan las demandas medico-legales, es posible que estos hallazgos conlleven una mayor responsabilidad legal para el facultativo en un futuro.

Figura 3

#### Relación Relativa de Riesgo Entre Diabetes y HLA

Grupo	LOCUS B		LOCUS D	
	B-8	B-15	Dw 3	Dw4
D.M.I.D.				
D.M.N.I.D.	2.21	2.60	6.40	3.70
	1.00	1.00	1.00	1.00

Según Soeldner, J.<sup>4</sup>

D.M.I.D.: Diabetes Mellitus Insulinodependiente

D.M.N.I.D.: Diabetes Mellitus no-insulinodependiente

## II. Genética Bioquímica e Ingeniería Genética

Los últimos cinco años han traído más avances a la genética bioquímica con técnicas de ingeniería que la trayectoria total en años de la genética bioquímica en sí. Técnicas desarrolladas en la última década, con cultivo de células y tejidos, de clonación, de híbridos y de inducción de procesos moleculares específicos hacen vislumbrar "la cura" para múltiples trastornos metabólicos de síntesis o de degradación.

Las perspectivas de escasez de insulina y el hecho de que para el año 1995<sup>14</sup> la demanda y la producción de insulina se igualarán en los Estados Unidos de Norteamérica, han hecho buscar otras alternativas terapéuticas, especialmente para los diabéticos dependientes de insulina. En estos últimos años la biosíntesis de insulina ha sido intentada con insulina de rata<sup>15</sup> y posteriormente con insulina humana. La producción teórica de insulina humana por bacterias de *Escherichia coli* es posible

con técnicas de recombinación de DNA. Obteniendo material ribonucleico con plásmidos (material de DNA) aislados de *E. coli*, e insertando estos a bacterias de *E. coli*, se producirá la insulina o su precursor (proinsulina) como se ha podido realizar con la insulina de rata.<sup>15</sup>

En septiembre de 1978, un grupo de investigadores del Centro Médico "City of Hope" de Duarte, California, y un grupo de Genetech, Inc., un laboratorio privado de San Francisco, California, informaron la inducción de síntesis de insulina humana en bacterias de *Escherichia coli*.<sup>16 17</sup>

Con técnicas de recombinación de DNA se logró inicialmente la producción de genes inductores de síntesis de insulina para la cadena A y B por separado. El proceso de síntesis conlleva el ligar genes de cadena sintética a plásmidos (material genético) de *E. coli* (por ejemplo betagalactosidasa) mediante un cordón de metionina. Este último facilitaría la purificación de la cadena polipeptídica en bromuro de cianógeno al producirse la proteína sintetizada. Después de un período de fermentación adecuada bajo condiciones de cultivo estrictas, se matan las bacterias *E. coli* con cadena A y B entretrejidas, extrayéndose posteriormente la proteína quimérica (ejemplo: betagalactosidasa-metionina-cadena A y betagalactosidasa cadena B). Se emplea bromuro de cianógeno para separar la cadena A y B de la betagalactosidasa. Se convierten las cadenas A y B a derivados S-sulfonados. Se purifican, se combinan ambas y el producto combinado, la insulina, se purifica aún más.

La técnicas de producción ha avanzado en los últimos dos años produciéndose la misma a nivel comercial en forma de proinsulina, en lugar de cadenas por separado, la cual es purificada y llevada a la forma activa. La producción de proinsulina a escala comercial está permitiendo noveles proyectos de investigación que redundarán en nuevos modos terapéuticos en cuanto a tipo y forma de administración de insulina. En un futuro no muy lejano estará a la orden del día el uso de preparados de mezclas de insulina y proinsulina, logrando distintos períodos de acción y efectos de las mismas.

La secuencia de aminoácidos de la insulina sintética humana de *E. coli* es similar a la insulina pancreática humana. Su actividad es comparable a la del páncreas de cerdo y la de insulina humana en ensayos radioinmunológicos, estudios de radioreceptores, y efecto hipoglucémico en conejos. La insulina producida es de calidad "purificada" y no contiene proteínas pancreáticas. Su reactividad a pruebas de pirogenicidad y endotoxinas es igual o inferior al encontrado en insulinas convencionales.<sup>18 19</sup>

Ya se han realizado las pruebas en humanos voluntarios con la insulina sintética de la Cia. Elli Lilly, observándose resultados favorables y ningún problema específico a la misma. Ello ha conllevado su aprobación para uso clínico libre en Inglaterra, adonde fue puesta en el mercado en noviembre de 1982. A partir de enero de 1983 su utilización libre será autorizada por el "Food and Drug Administration" de los Estados Unidos.

Seis patentes han sido solicitadas para el proceso de síntesis insulínica en Norteamérica. Otras proteínas que están siendo sintetizadas con técnicas similares incluyen somatostatina, hormona de crecimiento, interferon, además de otras proteínas, incluyendo la producción de antibióticos.

Diversos estudios clínicos han sido realizados en animales<sup>20</sup> y humanos para dilucidar su efectividad y acelerar su producción y uso por la comunidad diabética. Destacan los de Keen y colaboradores,<sup>21</sup> y los realizados por Galloway y colaboradores.<sup>22</sup>

Keen y colaboradores realizaron las primeras pruebas en humanos normales analizando las reacciones cutáneas locales y su efecto hipoglucémico mediante inyección subcutánea o endovenosa, comparándolas con insulina purificada porcina.

La inyección subcutánea no dió lugar a diferencias específicas en las reacciones locales observadas entre las dos insulinas. No se observan efectos adversos a corto plazo. Estudios respecto a alteraciones inmunológicas por administración prolongada están en desarrollo.

Ambas insulinas mostraron un efecto hipoglucémico familiar, pero la sintética humana produjo un efecto algo mayor en dosis bajas por las vías subcutáneas y endovenosas. Con toda probabilidad la insulina humana ejerce mayor acción a nivel hepático (inhibiendo la descarga de glucosa hepática) que a nivel periférico (donde aumentaría la captación de glucosa). Ello puede ser debido a una mayor extracción hepática por el hígado normal bajo el influjo de insulina humana que por la insulina porcina.

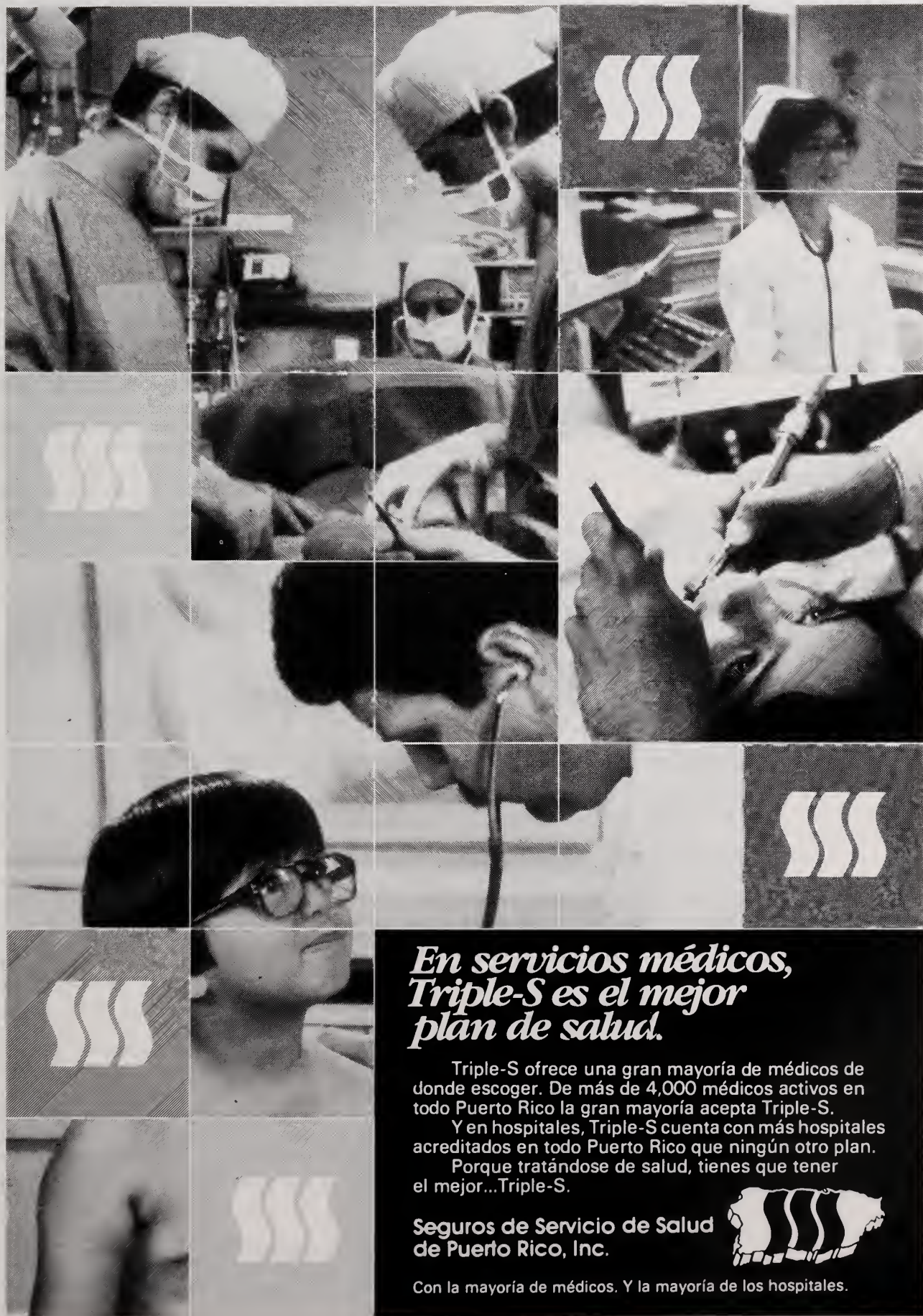
Los estudios en humanos muestran que la insulina sintética presenta propiedades muy similares a las purificadas de cerdo. Incluso el efecto antigénico en ambas insulinas es el mismo.<sup>22</sup> Recientemente, cuando presidimos la Sesión de Ingeniería Genética del Simposio Satélite del XI Congreso de la Federación Internacional de Diabetes, celebrada en Santiago de Compostela, España, pudimos intercambiar experiencias sobre la ingeniería genética con los investigadores de la Cía. Elli Lilly.

Desde los años 20 hasta el presente la terapia ha estado basada en la dieta e insulina. La insulina ha sido purificada y al presente sintetizada por bacterias. Confiamos que el futuro depare para el diabético la inducción de síntesis en sus propias células y así lograr una "cura" por técnicas de ingeniería genética. Mientras tanto tenemos la certeza de que en los próximos años mejoren los aparatos de infusión de miniatura.

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## The Medical Case For Ending Boxing

By George D. Lundberg, M.D.

The principal purpose of a boxing match is for one opponent to render the other injured, defenseless incapacitated, unconscious. No caring person could have observed the events in professional prizefighting in the past few months and not have been revolted. No prudent physician could have watched the most recent debacle/mismatch on Nov. 26, 1982, between Larry Holmes and Randall (Tex) Cobb, and believe that the current boxing control system is functioning. The fact that this massacre came on the immediate heels of even more tragic fights serves to accentuate the uncontrolled situation.

The American Medical Association recognized this problem some time ago, and its Council on Scientific Affairs commissioned a panel to study the problem and to make recommendations. The report, presented in this issue, is the official A.M.A. position. It is solid, balanced, and reasonable. It operates with the assumption that boxing cannot be stopped, so it recommends ways in which it should be controlled better. To continue its interest in the safety and medical care of boxers, the A.M.A. is co-sponsoring a conference with the Association of Ringside Physicians on "Medical Aspects of Boxing" at Caesars Palace Hotel in Las Vegas, Nev., on Feb. 18.

Eleven faculty members will discuss the duties and responsibilities of the ring physician, emergency medical procedures in the management of the severely injured boxer, and several other important topics.

Since the council report was approved by the A.M.A.'s House of Delegates in 1982, two other major studies have appeared. Kaste et al, writing in a recent issue of *The Lancet*, studied 14 boxers who had been national champions in Finland and who had been carefully screened and found not to have other known reasons for brain atrophy. They report computed axial tomographic (CAT) evidence of brain injury in four of six professional and one of eight amateur boxers. Also, two of the professionals and eight of the amateurs had electroencephalographic abnormalities that may have been caused by brain injury.

They state: "The most predictable and permanent reward... is chronic brain damage", and "*The only way to prevent brain injuries is to disqualify blows to the head*".

Appearing in the Jan 14 1983 issue of JAMA, Ronald J. Ross, M.D.; Monroe Cole, M.D.; Jay S. Thompson, M.D., and Kyung H. Kim, M.D., report a study of 38 boxers with

CAT scans, 24 of whom had a complete neurological examination and electroencephalograms as well. They report a significant relationship between the number of bouts fought and brain damage detected by CAT scan, and demonstrate no significant relationship with neurological symptoms or findings or number of knockouts or technical knockouts. This is additional strong evidence of chronic brain damage with cerebral atrophy in many fighters.

Some have argued that boxing has a redeeming social value in that it allows a few disadvantaged or minority individuals an opportunity to rise to spectacular wealth and fame. This does occur, but at what price? The price in this country includes chronic brain damage for them and the thousands of others who do not achieve wealth, fame, or even a decent living.

Others argue that man must fight and that surreptitious fights will occur if boxing is outlawed, producing an even worse situation. I suggest that such is equivalent to arguing that gunfighter duels should be instituted, ticknets sold, and betting promoted since, after all, homicide by gunshot is also common in our society.

Boxing is wrong at its base. In contrast to boxing, in all other recognized sport, injury is an undesired by-product of the activity. Boxing seems to me to be less sport than is cockfighting; boxing is an obscenity. Uncivilized man may have been bloodthirsty. Boxing, as a throwback to uncivilized man, should not be sanctioned by any civilized society.





# The Dimensions of Surgical Progress in Cardiac Surgery

by Dwight C. McGoon, M.D. FACS\*

Those of us who were born before the end of the first quarter of this century came into a world that had a narrow view of the potential of cardiac surgery, a view expressed by Stephen Paget just before the turn of the century. In 1896, Paget said that "surgery of the heart has probably reached the limits set by nature to all surgery." Now hundreds of thousands of heart operations of the widest variety are performed annually, at an estimated cost in this country alone of some \$4-billion dollars a year.

Therefore, this may be an ideal time to view the broad picture of cardiac surgery and its many interrelationships; in short, a time to discern the dimensions of surgical progress as exemplified in the subspecialty of cardiac surgery.

## The Temporal Dimension

The notion of surgical intervention directed at the heart is a relatively modern concept. At the end of the last century, Billroth commented: "Any surgeon who would attempt an operation on the heart should lose the respect of his colleagues." It seems ironically appropriate that in the same year, 1896, in which Stephen Paget had said that surgery of the heart had probably reached the limits set by nature to all surgery, the first successful operation on the heart was performed in Frankfurt am Main by one Ludwig Rehn. The operation was suture repair of a stab wound of the heart. So the critical exigencies of an otherwise fatal cardiac wound provided the impetus for the first surgical advance.

In the United States, the first cardiac operation is credited to Luther Hill, in Louisiana, in 1902, under similar circumstances as those of Rehn's operation. Surgery for cardiac trauma then progressed until it reached an advanced degree of development in World War II, as accomplished by Dwight Harken. His series of 134 operations, in which foreign bodies were removed from the heart and great vessels, represents a remarkable achievement. There were no deaths in this series and all of the patients left the chest centers with normally functioning hearts.

Major credit for the origins of the surgical management of intracardiac congenital defects belongs to Dr. Alfred Blalock who, in 1944, at Johns Hopkins, transformed a blue, severely limited youngster into a pinker and more active child by anastomosing the subclavian artery to the pulmonary artery. That startling breakthrough occurred during World War II.

A series of innovative palliative procedures followed, but the next most important step forward, and perhaps the most important of all, came with the successful completion in 1953 of an open-heart operation with the aid of a heart-lung machine. The operation and the machine are credited to that individual whom this lecture memorializes, Dr. John H. Gibbon, Jr. He closed an atrial septal defect.

Although Dr. Gibbon did not pursue the clinical application of his innovation further, others, like John Kirklin, seized the opportunity and carried forward its potential to the correction of large series of patients who had more common congenital cardiac anomalies, which included ventricular septal defect, atrioventricular canal, and tetralogy.

Because the space and opportunity within the heart for correcting certain of the more common congenital defects proved to be limited, Kliner, Kirklin, Donald Ross, Rastelli, and others came upon the idea of routing the overflow of the pulmonary ventricle through an extracardiac tunnel to the pulmonary circulation.

There remained a difficult group of patients characterized by underdevelopment or absence of one of the ventricles, and Fontan developed a scheme to use that ventricle as the systemic ventricle, while routing the systemic venous return by one of several possible connections directly into the pulmonary ventricle altogether.

Thus progress in congenital cardiac surgery has had four major phases: palliation, intracardiac correction, extracardiac conduit placement, and pulmonary ventricular exclusion. Pulmonary ventricular exclusion remains tentative because the long-term effects of this highly anomalous arrangement are not fully known as yet. Some recent, extended follow-up reports on the Fontan operation seem to fuel our fears, in that chronically subnormal cardiac output with poor improvement during exercise has been commonly observed.

## The Intellectual Dimension

Progress is mankind's great overbearing objective. The urge toward progress seems almost instinctive, something that is inherent and a primary premise, a genetic imperative, not something to be decided rationally. This seems to be singularly true of physicians. So the record of progress is the record of intelligence, of knowledge. This also holds true for surgery.

Alexis Carrel, early in this century, defined the act of conceptualization as being a function of intuition, which he defined as "the seemingly instinctive impulse of the scientist toward a discovery." We need not be a medical historian to recall some of the new concepts that totally reoriented an area of understanding. William Harvey's "seemingly instinctive impulse toward discovery" in conceiving of circulation as being circular is an example of such a startling new concept that comes easily to mind.

While an investigator at the Rockefeller Institute, Carrel himself achieved a landmark in surgery just after the turn of the century when he perfected the technique of anastomosis of small blood vessels. This technique has made many of the feats of modern surgery possible. In fact, Carrel, even at that time, was able to transplant organs in animals since he had developed the ability to anastomose vessels of two mm or so in diameter. A spin-off of his studies on transplanted organs was the cultivation, in glass, of the cells and tissues of

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warm-blooded animals. An important side-effect of this development was the ability to grow viruses outside the body in cell cultures. Appropriately, Carrel was awarded the Nobel Prize in 1912.

Concepts, then, are imaginative glimpses of reality, and the authenticity of these imaginative glimpses must thereafter be tested and retested against the truth of reality. Let us contrast the early concept of the circulation of the blood, first published three and a half centuries ago, to a current concept, dynamic spatial reconstruction, which is being studied by Drs. Earl Wood and Erik Ritman and their associates at the Mayo Clinic. The basic concept of dynamic spatial reconstruction is that the radiodensity of every cubic millimeter of the thorax can be determined 60 times per second by an elaborate array of up to 28 x-ray entrainments, and this vast information can be recorded, manipulated, and displayed through computer interaction. Immense investigative and clinical applications for such a device are conceivable.

### The Spatial Dimension

Every substance that we know of is made up of tiny units of matter and/or energy. The whole world is a complex construction of elementary particles, such as quarks and hadrons. Furthermore, there are quarks and antiquarks, and up, down, strange, and charmed quarks—all of this is beyond my capacity to understand. I can only comprehend that these units are arranged in ever increasingly complex combinations to constitute the universe about us.

They emerge from the unseeable at the level revealed by the electron microscope, where cells and their subcellular structures, in all of their complexity, can be identified, existing like little cities. A cardiac myocyte is a useful example. It is 11 microns in diameter. It has a complex city wall, or cellular membrane, which continually admits and expels a multitude of substances and responds through its receptors to the outside environment. The nucleus, or city hall, is a repository of information essential to survival and propagation. The mitochondria are factories for the transformation of substrates into usable energy. Transportation channels are provided by the tubules, and of course the myofibrils perform the function for which the cell exists.

We can only imagine what it would be like if this were a living miniature city instead of a pickled one: the hustle and bustle that must take place during every millisecond of each cardiac cycle; the hectic transportation of substrates and wastes, flowing electrons, and ions; the production of consumer goods; the perpetual convulsive contraction and relaxation. How utterly marvelous! One cannot help but wonder what force thought it up, and made it run, and tested it, and pushed it off into an eternity of automatic operation.

It was a major step forward in surgical progress when the issue of protecting, during operation, the structure and function of basic myocardial subcellular organelles was addressed. In the past decade, a vast amount of research has been devoted to the improvement of our ability to protect the delicate structural and functional integrity of these beautiful and intricate machines. The approaches have involved hypothermia, prompt electromechanical arrest, substrate enhancement, and drug additives to ameliorate reperfusion injury.

I am baffled and truly mystified by the observation that the arrested, nonperfused heart may be *better* protected than

the perfused, nonworking heart. What does this say about the blatant inadequacies of our present system of perfusion? What implications of this inexplicable injury of perfusion pertain to wholebody perfusion? Can the lessons of cardioplegia be a portent of something we might call corporoplegia, or "whole-body arrest"? If the heart is better protected during operation by the absence of perfusion, is it possible that whole-body arrest is also indicated? No doubt there is much to be learned concerning the methods of cardiopulmonary bypass and myocardial protection.

From this subcellular extent of the spatial dimension one can move up through the familiar macroscopic range of day-to-day operations—the ordinary spatial dimension of our lives—to valve replacements, coronary arteriograms, techniques for coronary bypassing, and all the daily decisions, technical judgments, and manipulations we make.

From the ordinary spatial dimension of daily practice, one could pass on to the other end of the spectrum, the cosmic dimension. We have no idea how many worlds there are out in space that might faintly resemble our earth and might have biologic units requiring a circulatory system, but we know that some five-billion such human biological units now exist on the beautiful planet earth, crowded and seething in the more habitable regions, being born and dying off, each appearing for a time and then ceasing to be.

And the most common cause for this ceasing to be, at least among the more developed societies, is a malfunction of the heart, by far the most common cause of death. Now cardiac surgery is surely not the sole means nor even the probable means for significantly lengthening the normal 70 or 80 years of human life. Nevertheless, this perspective of the spatial dimension with its attendant speculation that the average life span could be stretched by such advances as the control of heart disease leads to altogether new concepts. Is a stretched-out life expectancy indeed a worthy goal? How will we cope with the newly evolving social and economic problems of that gorgeous earth, which houses an aging population who must carefully protect against an overabundance of healthy, vigorous, energetic young people?

### The Transitional Dimension

If cardiac surgery can be characterized at all, it can be characterized by a propensity to change; it has a record of rapid transition. The very first stage of transition in cardiac surgery was in the 1940's, when the specialty transcended from almost nonexistence to an ability to palliate congenital heart disease by closed-heart operations. Three types of palliation became possible:

- Shunting procedures to increase pulmonary blood flow when it was inadequate, as exemplified by the Blalock-Taussig operation, the Potts operation, and Waterston-Cooley operation.

- Pulmonary arterial banding to decrease pulmonary blood flow when it was excessive, the Muller-Damman operation.

- Creation of an atrial septal defect to improve intracardiac mixing, the Blalock-Hanlon operation.

The early '50s saw limited *intracardiac* ventures through surface-induced hypothermia or the atrial well technique. The late '50s marked the transition to more or less unlimited access to the interior of the heart. Substitute valves came into use in the early '60s and complex cardiac anomalies yielded to the



surgeon by the late '60s. The '70s brought first the dramatic expansion of bypassing coronary arterial obstructions and then the maturation of the principles and importance of intraoperative protection of myocardial integrity.

In the future, when we look back upon the decade of the '80s, what transition will stand out? Will this be a decade of consolidation, of refinement in techniques and devices, and of greater precision in the timing and indications for surgical intervention? Will a resurgence appear in cardiac transplantation or an expansion of cardiopulmonary transplantation? Or will the artificial heart achieve clinical success? Or will some other breakthrough occur?

### The Financial Dimension

The demand for cardiac surgical services impacts the socioeconomic aspects of this field. In a study of a single, total, population unit, which included all of the population of Olmsted County, Minnesota, Kennedy et al found that the rate of operation for coronary artery disease increased from 15 per 100,000 population in 1973 to 40 per 100,000 in 1977. All other cardiac operations fluctuated around a steady rate of about 25 per 100,000 per year.

So the rate for all cardiac operations during those five years increased from 41 to 59 per 100,000 population. A more recent study of the same population unit by the same investigators showed a stabilization in the number of operations for coronary artery bypass since 1977. Data gleaned from the Commission for Professional and Hospital Activities and the National Center for Health Statistics from the entire United States show similar stabilization.

Since the apparent demand for coronary operations has hit a plateau in the last four years, and since the frequency of other types of cardiac operations has remained stable for many years, the rate for all open-heart operations has remained quite static for four years. This apparent plateau in the demand for cardiac operations in this country undoubtedly has far-ranging implications with respect to the financial dimension of cardiac surgery, implications involving surgical manpower, other health-care providers, the number of hospitals providing these facilities, and the health-care industry.

This plateau, which implies the possibility of a future downturn in the rates of cardiac operations, leads to conjecture as to cause or causes. With the advent of beta-adrenoreceptor blocking drugs, calcium slow channel blocking drugs, a wealth of new anti-arrhythmic medications, and other new drugs, some degree of validity may be given to the claim of Harvard's Dr. Bernard Lown that "an integrated medical program... can substantially reduce mortality, improve lifestyle, and equal the results of surgery if not supersede them."

While I am not aware of any statistics that claim a better survival for medical treatment than surgical treatment for most categories of patients with advanced coronary artery disease, nevertheless the apparent progressive improvement in survival from newer methods of medical therapy must be considered in any comparative analysis of results. The prevalence of recurrent symptoms now appearing in patients following percutaneous transluminal coronary angioplasty and the complication rate of the procedure suggest that the impact of this technique on the need for operative intervention may, in the long run, be quite limited.

Of particular interest is the probability that the incidence and risk of death from coronary artery disease in this country is declining. As reported in a study by Connolly et al, deaths due to coronary heart disease among residents of Rochester, Minnesota, reached a peak of 184 per 100,000 population in 1969 but since then deaths have fallen to 61 percent of that level, declining to 113 per 100,000 by 1978. This declining mortality from coronary heart disease is primarily attributable to declining mortality from myocardial infarction in recent years.

### The Valuational Dimension

In the cosmic view, all of our initiatives, research, education, administration, writing, editing, and long hours of intense labor at the operating table have *inherent*, fundamental, and transcendent value only in one respect, as an unselfish expression by trained, skilled, and dedicated surgeons of a concern for the welfare of a needful human being, the patient. It is an awareness of this simple single mission that we of the profession need today.

To recognize that the ultimate purpose of our endeavor is the expression and manifestation of compassion for suffering humanity gives orientation to our professional motivation, and gives hope and example to all of humanity.

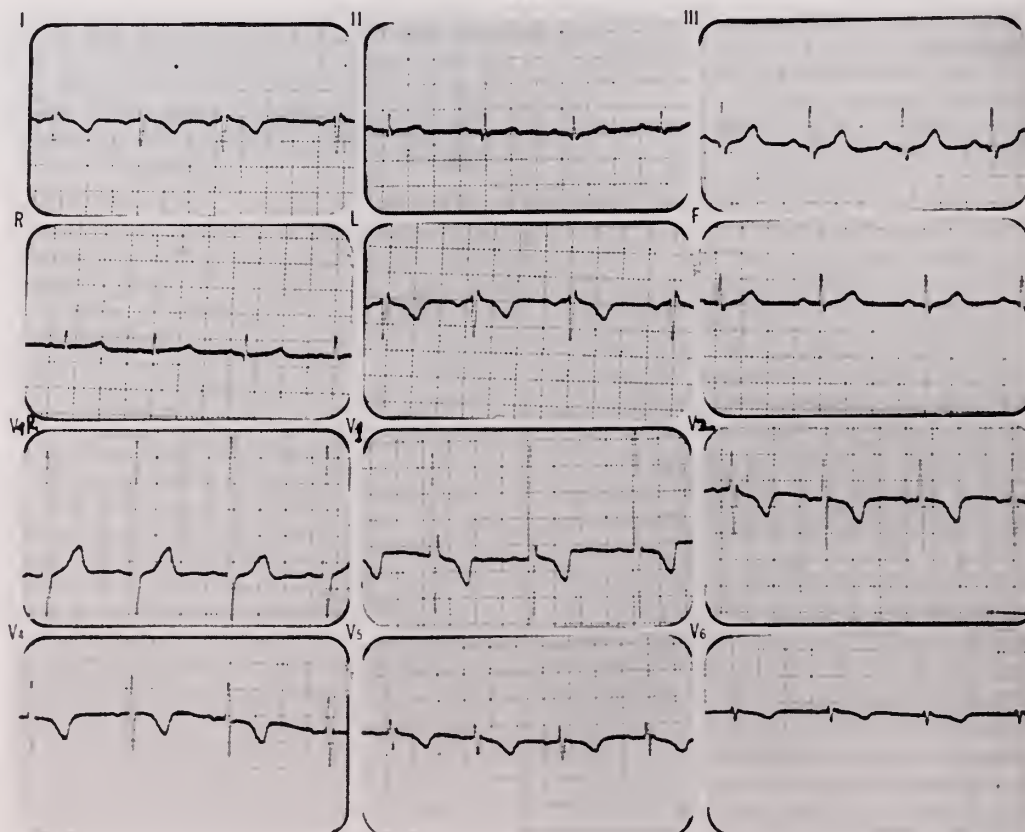
The John H. Gibbon Lecture. As published in the Bulletin of the American College of Surgeons. Vol. 67 (11);15, 1982.



## **ELECTROCARDIOGRAFIA PEDIATRICA**

**P**CD es una niña de 3 años de edad con un historial médico normal, asintomática, referida para evaluación cardiovascular de rutina por un soplo sistólico detectado por el médico escolar. La niña tiene crecimiento y desarrollo normal, está acianótica y su soplo se diagnostica como inocente.

Se obtuvo el siguiente electrocardiograma:



## **Sección de Autoevaluación**

El trazado electrocardiográfico demuestra:

- a) hipertrofia ventricular derecha
- b) hipertrofia ventricular izquierda
- c) dextrocardia congénita
- d) dextroversión cardíaca
- e) isquemia del miocardio

**Respuesta: c) Dextrocardia Congénita**

La dextrocardia es un concepto muy amplio, aunque literalmente significa que el corazón está localizado en el hemitórax derecho. Hay dos tipos principales de dextrocardia:

1. con *situs inversus* - además de inversión de las cámaras cardíacas hay inversión visceral.
2. con *situs solitus* - hay dextrocardia aunque sin inversión de las cámaras cardíacas ni visceral.



La *dextrocardia con situs inversus* es el tipo más frecuente. En ella las cámaras cardíacas están invertidas y la mayor parte de la masa cardíaca está en el lado derecho del torax. El apex cardíaco se localiza en el 5º espacio intercostal derecho a nivel de la línea medioclavicular derecha. Este tipo de dextrocardia siempre se asocia con *situs inversus* total y usualmente es no-complicada. No es frecuente su asociación a cardiopatías congénitas.

En la *dextrocardia con situs solitus* (dextrorotación) se conserva la relación anatómica de los atrios, sin embargo, los ventrículos están rotados hacia la derecha de manera que el apex también estará en la línea medioclavicular derecha. Como no hay inversión atrial tampoco ocurre la inversión visceral. Este tipo de dextrocardia casi siempre va asociado con cardiopatías congénitas. En 75% de los casos hay una cardiopatía congénita cianósante asociada.<sup>1</sup>

### Hallazgos Electrocardiográficos

En dextrocardia con *situs inversus* la derivación I es la "imagen en espejo" de la derivación I del corazón sin inversión de cámaras. La derivación III refleja los potenciales ordinariamente registrados en la derivación II y viceversa. De igual forma aVL registra los potenciales de aVR y viceversa.

En las derivaciones precordiales el V<sub>1</sub> refleja el trazado ordinario de V<sub>2</sub>, las derivaciones V<sub>3</sub>, V<sub>4</sub>, y V<sub>6</sub> demuestran las variaciones de potencial que suelen verse en V<sub>3</sub>R; V<sub>4</sub>R; V<sub>5</sub>R; y V<sub>6</sub>R.

Debe sospecharse dextrocardia con inversión de cámaras siempre que en un electrocardiograma aparezca:

- onda P invertida en la DI
- onda R dominante en aVR
- reversión en la progresión del voltaje desde V<sub>1</sub> a V<sub>6</sub>

En presencia de los hallazgos electrocardiográficos descritos el ECG debe repetirse intercambiando los cables de los brazos entre sí, haciendo lo mismo con los cables de las piernas. Una vez hecho esto, se registran las derivaciones precordiales desde la izquierda hacia la derecha, o sea, desde V<sub>2</sub> y V<sub>1</sub> hasta V<sub>3</sub>R; V<sub>4</sub>; V<sub>5</sub>R; y V<sub>6</sub>R. El ECG resultante se interpreta entonces como el de una persona con *situs solitus* cardíaco.

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### ¿QUE ES LA FUNDACION MEDICA DE PUERTO RICO?

Con el fin de mejorar los servicios y facilidades médico-hospitalarias y de salud en nuestro país se ha organizado la Fundación Médica de Puerto Rico bajo los auspicios de la Asociación Médica de Puerto Rico. Esta institución se sostendrá con fondos que proveerán otras organizaciones similares, grupos de la comunidad, y, en particular, la clase médica de Puerto Rico.

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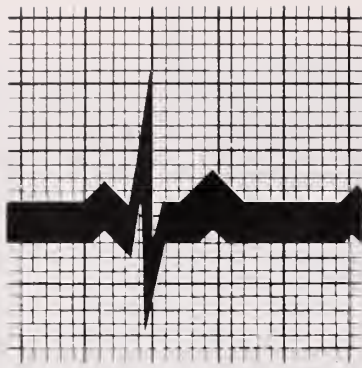
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Los propósitos de interés inmediato para la Fundación Médica de Puerto Rico son:

1. Fomentar los proyectos para la construcción de hospitales para la comunidad.
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3. Establecer un servicio de localización de médicos para mejorar la distribución de doctores en todo el país.

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AL SERVICIO DE LA PROFESION MEDICA  
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# ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD, FACC

This 30-year-old female gave a history of a heart murmur and acrocyanosis since early childhood. Cardiac catheterization and heart surgery were refused. In January and February, 1981, she presented with dizziness, marked dyspnea, orthopnea, clubbing of the fingers and toes, perioral and acrocyanosis. She was taking digoxin. The pulse rate was 110 per minute. A grade 11 harsh systolic murmur was heard at the left sternal border, second inter space, which radiated to the neck and cardiac apex. Hemoglobin was 17.3 g and hematocrit 55%. Arterial blood gases (room air) revealed a  $pO_2$  of 27.5 and  $pCO_2$  23.5 mm Hg,  $HCO_3$  14.6 meq/L, pH 7.44. The chest roentgenogram showed right ventricular enlargement (RVE) with an uplifted apex, prominent main and left pulmonary arteries (LPA) and slightly decreased pulmonary vascularity. An echocardiogram supported the clinical diagnosis. The patient received oxygen by mask. On February 20, 1981, she suffered cardiac arrest and expired. See Figure 1.

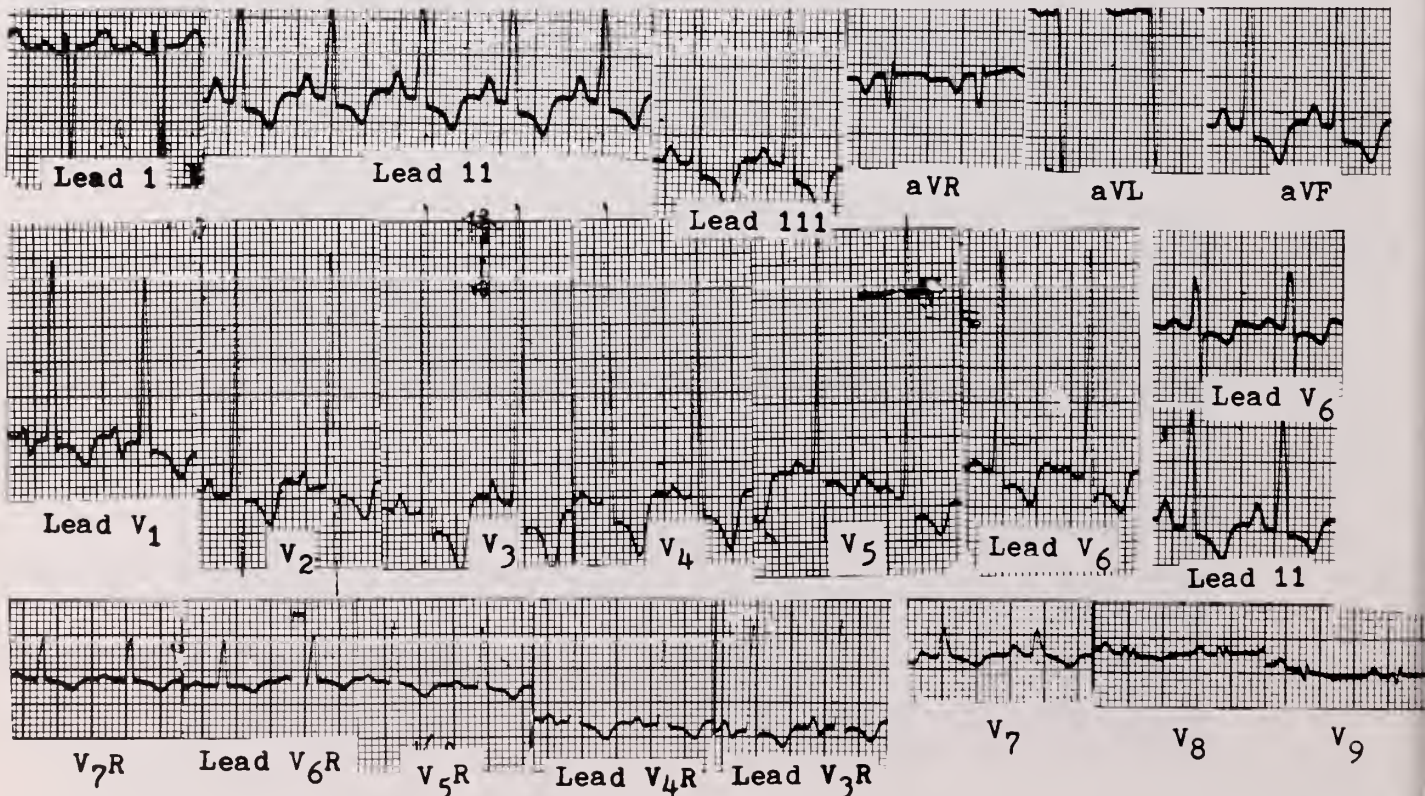
## Questions

1. What are the electrocardiographic diagnoses?
2. What is the clinical diagnosis?
3. What is the pathogenesis of this presentation?

## Post Mortem Findings

Congenital valvular pulmonic stenosis (PS)  
 Poststenotic dilatation of the pulmonary trunk and LPA.  
 Patent Foramen Ovale (PFO) - opened to 0.4 cm.  
 Cardiomegaly, 500 g.  
 Signs of congestion.  
 Intact interventricular and interatrial septi.  
 Measurements: right atrium (RA) 0.2 cm, right ventricle (RV) 1.2 cm., left atrium (LA) 0.3 cm., left ventricle (LV) 0.9 cm., pulmonic valve 3 cm, 3 cusps, severely deformed thickened, calcified.

Figure 1





## Electrocardiogram

Axis + 110° marked RA enlargement, possible LA enlargement, (negative P wave in  $V_1$ ). Marked RVE, pressure overload. Large predominant R complexes exist from lead  $V_7R$  to  $V_7$ . These tall R waves in  $V_{4-7}$  suggest LV hypertrophy. Even  $V_9$  shows as small  $rsr'$  complex. A septal q wave denoting LV forces is not observed in any left precordial lead. There are marked ST segment depressions and T wave inversions in the inferior leads and all the precordial leads, indicating overwhelming RV strain and systolic overload. Lead  $V_6$  (and lead II) appearing in only one ECG shows the more typical R/S pattern of PS. Another unillustrated trace demonstrated an R wave in  $V_5$  of 45 mm and in  $V_6$  of 33 mm amplitude. See figure 1.

## Discussion

This patient demonstrated severe PS, a PFO and marked arterial desaturation with cyanosis and clubbing. Right-to-left shunting at the atrial level via the PFO can explain the pathophysiology.

However, the ECG is not that usually observed with severe PS. How can such tall R waves in the left precordial leads be explained? Associated defects causing LV hypertrophy were not present at autopsy. PS or atresia with intact ventricular septum, Type I, with some decrease in RV size, can produce LV dominance with relatively tall left precordial R waves or equiphasic R/S complexes in the mid and left precordial leads. Left axis deviation can occur in infants with pulmonary artery stenosis and the rubella syndrome. Usually lead  $V_6$  in severe PS shows a R wave with less amplitude than the S wave; yet, the R wave can be fairly well developed.

Morgagni, in 1761, described PS and a PFO in a 16-year-old female. Right-to-left interatrial shunting with a PFO or

an atrial septal defect has subsequently been referred to as "Trilogy of Fallot." This may overload the LA and LV, but it usually produces an ECG similar to that of isolated severe PS, illustrating: P waves of increased duration and amplitude in lead II, ST elevation in leads I and aVL, tall peaked T waves in leads I, aVF,  $V_{5-6}$ , a right bundle branch block pattern,  $S_1S_{II}R_{III}$  pattern or right, superior, posterior QRS, a Q in leads I and  $V_6$ , and a better developed R in  $V_6$  which may be larger than the S wave.

Paul Wood has reported an isolated example of a patient with congenital PS and an atrial septal defect who demonstrated LV hypertrophy and left axis deviation.

Sometimes in marked PS the very tall R waves present in leads  $V_{1-2}$  may extend up to  $V_6$  and only in  $V_7$  or  $V_8$  would equiphasic complexes be encountered. The T waves may remain inverted and discordant from  $V_4R$  to  $V_5$ . However, the ECG in this case is not completely explained by these considerations. Such huge R waves must be very rare in severe PS.

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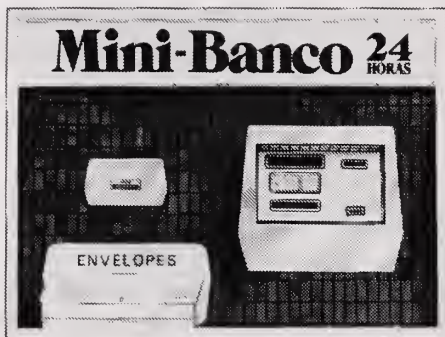
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\* From an Australian Heart Foundation pamphlet.

\*\* Information taken from the US Surgeon General's report: Smoking and Health, 1979.

\*\*\* British Medical Journal, 11th August 1979.

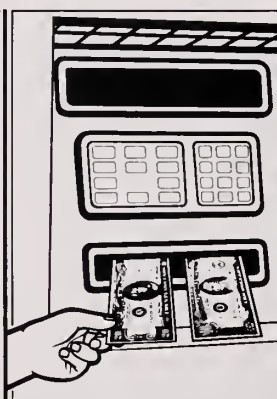
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## IMPORTANCIA DEL DELEGADO PARTICIPANTE

El mantenimiento de los principios de vida democrática en una institución requiere vigilancia, trabajo y sobre todo participación. La Asociación Médica de Puerto Rico no es una excepción y la misma se revitaliza en la medida que sus miembros participen en las deliberaciones y los procesos que dan origen a la política pública de la institución.

La participación efectiva de los socios no sólo requiere el estudio previo de los asuntos de importancia, si no también de la asistencia regular a todas las reuniones. Así mismo el interés que los presidentes de las distintas unidades organizacionales se tomen en mantener el número máximo de delegados en derecho a voz y voto, dará una oportunidad mayor a que su área o distrito, pueda balancear adecuadamente posiciones divergentes sobre un mismo asunto. En la buena democracia la discrepancia legítima es saludable y provechosa y no da origen a hostilidades, resentimientos o frustraciones personales.

Uno de los medios por lo cual una organización puede con más rapidez hacerse innecesaria en una comunidad o peor, tomar posiciones que no representen un balance adecuado entre sus intereses y los de dicha comunidad, es el que se propicie un desbalance de participación de los delegados, que representando su matrícula, establecen la política institucional. Si este desbalance se promueve activamente y se perpetúa, asumiendo solamente un sector o grupo de la institución el poder decisorio, fácilmente la institución puede irse gradualmente separando de la realidad que le rodea, al reflejar las decisiones de política institucional, solamente los intereses de algunos de sus miembros. Los delegados son líderes y la función de liderazgo, grupal o individual requiere comunicación continua a todos los niveles y consenso de opiniones para así tomar las mejores decisiones y lograr la aceptación genuina de las mismas en la asociación y la comunidad a la que pertenecemos.

Una de las formas más efectivas de evitar el enajenamiento social de una institución, es el que se les facilite a los delegados de las distintas unidades administrativas, poder analizar con tiempo los issues importantes y que estos puedan lograr un consenso para defender las posiciones que representen la forma de pensar de cada uno de los distritos o unidades. Es sólo a través de un balance adecuado de ideas distintas, en un ambiente que propicie el poder diferir, que se consigue que las conclusiones finales, como resultado de un proceso participatorio democrático, sean las mejores decisiones. Este proceso garantiza que las decisiones representen un balance apropiado entre los intereses de la institución y las necesidades de la comunidad a la cual sus miembros les brindan servicios. A su vez se evita el que la institución pierda prestigio al perder credibilidad o peor aún, se considere como una fuerza regresiva en contra de los mejores intereses de la comunidad en general. Todo delegado debe estar siempre consciente que la mejor manera de defender los intereses de nuestra Asociación es armonizando los mismos con el bienestar general de la comunidad.

Fue en gran medida el que se facilitara el mantenimiento de los principios arriba mencionados durante el pasado año, el logro más importante, de las personas que ejercieron su liderato a través de los distritos de la Asociación Médica de Puerto Rico.

Se han reafirmado unos principios. Se ha propiciado la participación. Se han abierto los canales para facilitar la incorporación de los Delegados de todos los distintos distritos en las posiciones importantes de la Asociación Médica. Se ha desarrollado el proceso lógico de que los delegados, primero se ganen el respeto de sus distritos y logren su respaldo para que luego puedan tener la oportunidad de asumir posiciones de liderato a nivel central con el apoyo de la mayoría de los distritos.

Los logros son evidentes y ahora es importante que se mantengan los principios mencionados. Es importante que los delegados de los distritos reconozcan la seria responsabilidad de que van a participar en las Cámaras de Delegados, representando una posición de su distrito sobre los issues importantes. Que sobre estos issues no van a depender de su propia opinión, ya que estos son muy complicados para que se dependa de opiniones espontáneamente creadas, sin el proceso de análisis adecuado. En este aspecto, el delegado como cualquier líder, tiene que oír y entender a los demás, tiene que mantenerse abierto a revisar sus posiciones personales sin sentir que se menoscaba su participación.

Es importante que los Delegados en sus respectivos distritos estudien detenidamente los issues de mayor interés que se van a discutir en la próxima cámara. Es fundamental para el bienestar de la institución que la discusión de los mismos, sea amplia y profunda y se logre un consenso que será representado por los delegados al reunirse la Cámara de Delegados. Así igualmente es importante, que cada uno de los delegados de los distintos distritos se mantenga en contacto con el mayor número de miembros de su distrito, para palpar directamente la posición de éstos sobre los asuntos de mayor importancia. Hay que saber cómo piensan los socios en cada distrito a la vez que se les mantiene informados de las acciones llevadas a cabo a nivel directivo.

Conociendo la tendencia al individualismo en los miembros de la profesión médica y creyendo que esta fuerza es esencial para que se pueda ejercer bien la profesión, que trabaja con decisiones de vida o muerte; es importante que todos los delegados comprendamos la definición de la palabra delegado.

Delegado es la persona a la cual se le transfiere o delega la facultad, autoridad o el poder que pertenece a otra. Siguiendo esta definición es claro que el delegado tendrá que seguir instrucciones con relación a la posición que asumirá en ciertos asuntos fundamentales y de gran interés para sus representados. Si el delegado no puede aceptar el representar los intereses de su organización puede poner en peligro los intereses de aquellos que tiene el verdadero poder; la matrícula total de la institución. Cito del Manual de Procedimientos Parlamentarios de Reece B. Bothwell página 23, Instrucciones a los Delegados: "por otro lado, cuando el delegado no recibe instrucciones sobre los asuntos fundamentales y de mayor interés para sus representados, se le concede una libertad casi absoluta lo cual resulta por lo menos, arriesgado".

El ofrecimiento de instrucciones obviamente, debe ser el resultado de un análisis amplio y profundo, a nivel de los distintos distritos de los issues de importancia, para así

lograr un consenso, el cual se espera que los delegados representen en la Cámara de Delegados debidamente constituida. ¿Cómo puede el Delegado evitar la sensación de que va a ser un instrumento o un altoparlante de opiniones de un grupo y no de un balance adecuado entre su criterio y el de los demás? La única solución es que el delegado participe activamente en la discusión de los issues en su distrito. Si después de dicha participación no puede convencer a la mayoría de su posición, debe acatar y respetar la posición de la mayoría y defender dicha posición en la Cámara de Delegados, en la cual estará él, representando la opinión de 30 médicos de su distrito.

¿Qué hacer si se da la situación en que un delegado, aunque ha tratado y se ha esforzado genuinamente por convencer a sus compañeros de que asuman una posición distinta sobre un issue, éste no logra hacerlo, pero tampoco es convencido por sus compañeros de la sabiduría de la posición de la mayoría? En esta situación consideramos que el delegado tiene dos opciones. Una discutir luego a nivel individual con sus compañeros en detalles la diferencia entre su posición y la de la mayoría, para tratar de lograr a través de una comunicación más prolongada, su propio convencimiento. En ausencia de esto, debería declarar a su distrito que con relación al issue que se ha discutido, él no podrá defenderlo activamente y solamente se limitará a votar a favor de la posición de su distrito.

De darse la situación en la cual el delegado en forma consistente considera que sus posiciones, que representan según su criterio las de la matrícula de la institución, no son aceptadas y además descubrir que son varios los delegados que se están sintiendo en dicha forma, puede entonces compartir ideas con sus compañeros. Deberá analizar los factores que les están impidiendo ser efectivos y tratar de lograr, a través de hacer conciencia a otros miembros, el que se revisen los procedimientos para que los principios que enumeramos inicialmente se garanticen y así revitalizar la institución a la cual pertenecen.

En otras palabras en nuestro sistema democrático siempre hay formas de lograr que nuestras instituciones representen los verdaderos intereses de la mayoría de los miembros, pero obviamente se requiere cierto grado de pérdida de libertad a nivel individual, por el logro de los intereses colectivos. Esta pérdida de libertad individual no implica paternalismo ni servilismo, pues la democracia es y siempre será, diálogo intenso y continuo, acción, revisión y lealtad a valores y principios institucionales que en última instancia sólo podrán responder a aquellos del pueblo al cual todos pertenecemos.

**J.A. Nuñez López, M.D.**  
Presidente Cámara de Delegados  
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# Medicolegal Decisions



## MINORS CAN SUE FOR LOSS OF PARENT'S COMPANIONSHIP

A minor child can sue independently for loss of the society and companionship of a parent wrongfully injured by a third party so as to significantly disrupt or diminish the parent-child relationship, the Iowa Supreme Court ruled.

A mother of three children, in the late stages of pregnancy, was treated at a hospital for bronchitis and hyperventilation. Allegedly because of improper diagnosis and treatment the patient suffered respiratory and cardiac arrest. As a result, she had severe, permanent brain damage and permanent blindness. Her fetus, which was nearly full term and capable of being born alive, was stillborn.

The patient brought an action against the hospital and physicians, seeking damages for her own injuries and for loss of services and support to her husband and children. Her husband sought damages for loss of consortium and medical expenses. The patient's three minor children sought recovery for "loss of family relationship, loss of companionship and association, the care, attention, kindness, maternal guidance, comfort and solace of their mother's society." The patient's husband also sued for the wrongful death of the fetus. The trial court dismissed the children's suit and the suit for wrongful death.

On appeal, the court pointed out the growing trend to recognize that minor children have independent identities and possess certain rights of their own. The court said that to recognize a right of recovery for a parent's loss of a child's consortium but not for a child's loss of a parent's is to fail to recognize that in any disruption of the relationship, the child probably suffers most. Finding that the reasons for recognizing the children's cause of action outweighed any problems presented, the court held that the minor children had an independent cause of action, with damages limited to the period of minority.

Finally, the court held that a fetus was not a person within the meaning of the law and affirmed dismissal of the wrongful death portion of the suit. The court sent the case back for further proceedings. —*Weitz v. Moes*, 311 N.W. 2d 259 (Iowa Sup. Ct., Oct. 21, 1981).

## GOOD SAMARITAN LAW NOT APPLICABLE IN ANGIOGRAM PATIENT'S SUIT

A jury should decide questions of negligence concerning the actions of a neuroradiologist who was called in to assist during an angiogram, a Georgia appellate court ruled.

A patient's physician had difficulty in maneuvering the catheter from the left carotid to the right carotid artery. He called in the neuroradiologist, who performed the maneuver with a little difficulty. He then left the room and had no further contact with the patient, who had a stroke about 15 minutes after completion of the angiogram. The stroke left him with permanent total paralysis of the left arm and hip and with permanent partial loss of the use of the left arm and hand.

A trial court granted summary judgment for the neuroradiologist on the basis of the Good Samaritan Statute. An appellate court reversed, saying that "as a matter of law, the hardship encountered here during the progress of the diagnostic procedure being conducted by an experienced physician did not constitute such an accident or emergency as would invoke the provisions of the Good Samaritan Statute." The physician then filed a second motion for summary judgment for him on the claim of negligence but denied it on a claim of battery and trespass for performing the procedure without the patient's consent.

On appeal, the appellate court reversed the judgment for the physician. A jury should resolve several questions of fact that were raised by the evidence, the court said. They included (1) Once the neuroradiologist took over the performance of the medical procedure for a brief period of time without the patient's consent, did he owe the patient the same duty that a treating physician owed his patient? (2) If so, was he negligent in failing to monitor the patient's condition? (3) Did the patient become unconscious during the angiogram and, if so, should the neuroradiologist have detected it? (4) Was he negligent in failing to follow the progress of the patient or to notify hospital officials that he had been involved in performing the procedure so that he could have been summoned when the patient's stroke was discovered?

The issue of negligence should be decided by a jury, the court concluded.—*Gragg v. Spenser*, 284 S.E. 2d 40 (Ga. Ct. of App., Sept. 11, 1981).

## PATIENT SUES FOR ALLEGED UNNECESSARY SURGERY

A patient may introduce evidence to show that a physician had performed unnecessary surgery on other patients, a New York trial court ruled.

The physician performed a lumbar laminectomy on the patient in 1972 and a cervical laminectomy in 1974. In a malpractice suit against the physician's estate, the patient claimed that the operations were unnecessary and that surgery was contraindicated. She contended that he had performed numerous operations on other patients and that those operations were also unnecessary and contraindicated. The patient sought an order permitting her to introduce evidence concerning the other operations to establish a common scheme or plan on his part. The physician's estate objected.

The court noted that about one dozen other cases were pending against the physician's estate and that similar allegations were made in some of them. The patient should be allowed to introduce evidence of prior operations on other patients for the limited purpose of proving a common plan or scheme on the physician's part to perform unnecessary and contraindicated operations. The estate argued that the evidence would be unduly prejudicial to it, but the court said that all evidence entered by the patient would not be used to prove that the operation on the patient was in fact unnecessary or contraindicated, the court said. —*Cotgreave v. Public Administration of Imperial County*, 443 N.Y.S.2d 971 (N.Y. Sup. Ct., Sept. 17, 1981).

#### OTHER PATIENT'S TESTIMONY NOT ADMISSIBLE IN SUIT FOR ALLEGED MALPRACTICE

Testimony by a former patient that she had never been advised prior to surgery that an unsuccessful stapedectomy could result in a hearing loss was inadmissible in a malpractice action by a patient claiming lack of informed consent, a Michigan appellate court ruled.

A physician specializing in otolaryngology diagnosed the patient's condition as otosclerosis. He advised her that her condition could be corrected by a simple procedure known as a stapedectomy. The patient claimed that the physician did not advise her that there was a possibility that the surgery could result in a hearing loss. The physician testified that he discussed the possible risks with her on several occasions. The operation was performed on June 11, 1973, and as a result she suffered a complete loss of hearing in her right ear. In a malpractice suit against the physician, a jury returned a verdict of no cause of action in favor of the physician.

On appeal, the court affirmed the decision. The physician testified that he informs his patients that his failure rate was just below five per cent. The jury was informed that the physician had performed six stapedectomies while in the service, about 14 more during his residency, one while in practice at a clinic, and one other one six months prior to the patient's operation. The operation prior to the patient's was also a failure.

The patient offered to call the former patient to testify that she had never been advised that an unsuccessful stapedectomy could result in a hearing loss. The trial court disallowed the testimony, saying that one prior incident of alleged failure to inform a patient did not establish that he had a "habit" of failing to advise. —*Cook v. Rontal*, 311 N.W.2d 333 (Mich. CT. of App., Sept. 9, 1981).

#### UROLOGIST LIABLE TO PATIENT FOR BREACH OF WARRANTY

A judgement of \$75,000 against a urologist based on his breach of warranty of successful operation to remove a diverticulum of the urethra should be affirmed, a District of Columbia appellate court ruled.

The patient's gynecologist referred her to the urologist for treatment. He recommended a diverticulectomy and allegedly told the patient and her husband that it was a simple operation without complications, that it would only temporarily interfere with their sexual relations, and that it was a safe operation. The patient consented to the operation, and it was performed on March 3, 1976.

After the operation, a fistula developed in the wall of her urethra at the site of the diverticulectomy. The urologist operated on her again in June 1976, in an unsuccessful attempt to close the fistula. A third operation, performed by another physician in November 1977, resulted in some improvement, but the fistula remained. As a result, she suffered from an uncontrolled discharge of urine, and the fistula affected her sexual relationship with her husband.

In a suit against the urologist, the patient sought damages for the complications from the operation and her husband sought damages for loss of consortium. The claims were both based on breach of warranty. They contended that they were induced to consent to the diverticulectomy by the urologist's express warranty that the operation was safe and that there would be no complications. The jury returned a verdict for the patient for \$55,000 and for her husband for \$20,000.

Affirming the decision, the appellate court said that the trial court properly instructed the jury on the applicable law. The court instructed the jury that it must find by a preponderance of evidence that the urologist "clearly and unmistakably (gave) a positive assurance (that he would) produce or... avoid a particular result or results in treating the patient." The court said no separate consideration was necessary to enforce the warranty claims because they were made prior to surgery and to induce consent to surgery.

Further, the husband's loss of consortium claim was appropriate, since he was personally assured by the urologist that the operation would interfere with their sexual relations only temporarily, the court said. —*Scarzella v. Saxon*, 436 A.2d 358 (D.C.Ct. of App., Oct. 2, 1981).

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### GOVERNMENTAL IMMUNITY APPLIES TO PSYCHIATRISTS AT PSYCHIATRIC CENTER

Psychiatrists' functions in evaluating the mental condition of a person acquitted of a criminal charge by reason of insanity were protected from liability by governmental immunity, a Michigan appellate court ruled.

A man who allegedly set fire to a house was adjudged incompetent to stand trial and committed to a psychiatric center. He was later judged competent to stand trial and found not guilty by reason of insanity. He was returned to the center, where two psychiatrists certified that although he was mentally ill he was not dangerous to himself or other persons. Less than four months after his release from the center, the man shot and killed a police chaplain and seriously injured another police officer.

The injured officer brought an action against the psychiatrists, alleging that they had negligently released the man and that their negligence was a proximate cause of his injuries. The trial court granted a motion to dismiss, finding that they were immune from liability.

On appeal, the court found that the officer had not shown that the psychiatrists had a higher duty of care toward police officers than toward the public at large. The court said that the center's function of evaluating the mental condition of persons acquitted of criminal charges by reason of insanity was created by statute, performed solely for governmental purposes, and had no corresponding equivalent in the private sector.

Therefore, the center performed a governmental function and the personnel employed by it were acting within the scope of governmental immunity.

The officer contended that the psychiatrists' functions at the center were ministerial in nature. The court responded that a ministerial function is one where his conduct is delineated. The court pointed out that where psychiatrists are required to make decisions regarding the state of a person's psyche and his liberty, such decisions require the ultimate in discretion and cannot be said to be ministerial in any sense of the word. Therefore, the court found that the psychiatrists were protected from liability by governmental immunity. —*Fuhrmann v. Hattaway*, 311 N.W.2d 379 (Mich. Ct. of App., Sept. 10, 1981; rehearing denied, Oct. 27, 1981, Nov. 4 1981).

### PATIENT SUES PHYSICIAN-ATTORNEY FOR ALLEGED LEGAL MALPRACTICE

A trial court erred in striking a claim for punitive damages against a physician-attorney in a legal malpractice action, a California appellate court ruled.

The patient had retained the physician-attorney to file a medical malpractice action against a hospital and others. The suit was filed more than a year after the patient learned of his injuries. The medical malpractice action was dismissed with prejudice for failure to prosecute.

The patient then filed a legal malpractice suit. The patient claimed that his attorney was negligent in failing to file suit within the statute of limitations, failing to actively pursue the case, to conduct discovery, to notify the patient of problems with the case, or to respond to his request for settlement. He also asserted a claim for punitive damages, contending that his physician-attorney was aware of the patient's pain and need for remedial surgery and that permanent injury would and did result. Nevertheless, the patient claimed, the physician-attorney advised him to forego surgery to increase the monetary value of the medical malpractice case and continued to advise against surgery even after he knew that he had failed to file suit within the statutory time limit.

The physician-attorney moved to strike the punitive damage claim, and a trial court granted the motion. On appeal, the appellate court said that the patient stated a valid claim for punitive damages. The alleged behavior by the physician-attorney demonstrated a conscious disregard for the patient's safety, the court said. A jury must determine whether in fact the attorney's possession of a medical degree and his alleged special awareness of the medical consequences of his legal advice constituted conscious disregard of his safety, the court concluded.

The appellate court ordered the trial court to vacate its order striking the punitive damage claim. —*Blegen v. Superior Court of Los Angeles County*, 178 Cal. Rptr. (Cal.Ct. of App., Nov. 23, 1981).

### MD's LICENSE REVOKED DUE TO INCOMPETENCE

The Commission on Medical Discipline properly revoked a physician's license to practice medicine because of professio-

nal incompetence, the highest court of Maryland ruled.

The Commission initiated its investigation of the physician's professional conduct as a result of newspaper accounts of his arrest on charges of committing a sexual offense involving a woman patient. The physician was acquitted of the criminal charges after a jury trial, but the Commission filed a report finding him professionally incompetent in a number of designated areas. It found that his medical records were inadequate; his prescription practices were medically unacceptable; that he used laboratory tests inappropriately; that his medical care did not reflect an orderly, thoughtful and logical approach to medical diagnosis and treatment; that his knowledge and clinical skills were medically unacceptable and that care provided to 16 specified patients was not medically acceptable.

After a hearing, the commission revoked his license to practice medicine. A city court stayed the revocation order, and the Commission appealed. The high court upheld the Commission's revocation of the physician's license. The physician did not contest the Commission's findings of professional incompetence, but instead contended that his due process rights were violated by the composition of the Commission and the procedures it followed. The high court rejected those arguments and upheld the revocation order. —*Commission on Medical Discipline v. Stillman*, 435 A.2d 747 (Md.Ct. of Apps., Oct. 9, 1981).

#### REMOVAL OF BULLET FROM ARRESTED MAN SHOULD BE CONSIDERED BY PHYSICIANS

A trial court should have granted the state's request for appointment of a physician panel to examine a criminal defendant and report on the feasibility of surgical removal of a bullet from his head, the Louisiana Supreme Court ruled. The defendant was charged with the murder of his wife. The state alleged that a bullet imbedded in the defendant's head was important evidence in the prosecution of the case and requested the court to order him to submit to a medical examination. At a hearing, a forensic pathologist testified that the bullet was located between the scalp and skull and noted that it could be moved about with pressure from a finger and that to do so did not appear to cause any pain. He concluded that the bullet could be removed under a local anesthetic with minimal risk. A trial court denied the motion, but the Supreme Court reversed. The request for a three-physician feasibility examination was reasonable and likely to afford the defendant protection of his rights and health. The state made a well-reasoned and commendable effort to establish a basis for searches of this kind, the court noted. —*State of Louisiana v. Martin*, 404 So.2d 960 (La Sup. Ct., Sept. 28, 1981).

#### FEDERAL COURT RULES ON FLORIDA MEDICAL PRACTICE ACT'S ABORTION REQUIREMENTS

The requirement in the Florida Medical Practice Act that a married woman notify her husband prior to obtaining an abortion was constitutional, but the requirement that a court

disregard the maturity of an unmarried minor in deciding whether to authorize an abortion was unconstitutional, a federal appellate court for Florida ruled.

A physician who performed abortions filed a class action challenging the constitutionality of several provisions of the Act. The Act required an unmarried minor to have either the written informed consent of a parent, custodian or legal guardian or a court order prior to obtaining an abortion. A wife who is not separated or estranged must furnish her husband with notice of the proposed abortion to allow him the opportunity to consult with her on the procedure. A trial court ruled that both requirements were unconstitutional.

On appeal, the court said that the provision permitting a court to base its decision on an abortion for a minor on what it found to be the best interests of the minor, regardless of the minor's maturity, was unconstitutional.

The provision relating to spousal notification was valid because of the state's interest in maintaining and promoting the marital relationship and protecting the husband's interest in the procreative potential of marriage. The notification requirement was not defective because it did not require a married woman to notify her husband of an impending hysterectomy or tubal ligation, the court said.

The case was remanded to the trial court for further proceedings. —*Scheinberg v. Smith*, 659 F.2d 476 (C.A.5, Fla., Oct. 2, 1981).



# Resúmenes de La Literatura Médica

**RECTAL SPARING IN ANTIBIOTIC-ASSOCIATED PSEUDOMEMBRANOUS COLITIS: A PROSPECTIVE STUDY.** FJ Tedesco, JK Corless, RE Brownstein. *Gastroenterology* 83:1259-1260, 1982.

Los autores evaluaron la frecuencia de pseudomembranas en el recto en pacientes con colitis pseudomembranosa asociada al uso de antibióticos. Estudiaron a 22 pacientes con este tipo de colitis. Diecisiete de 21 (77%) tenían pseudomembranas en los últimos 25 centímetros de colon (en el rectosigmoide). En tres (13.6%) se encontraban las pseudomembranas entre 25 a 60 cm. del ano. En la mayoría de los pacientes con colitis asociada al uso de antibiótico se pueden documentar las membranas inflamatorias con el sigmoidoscopio rígido; en otros el envolvimento puede ocurrir más proximalmente en el colon.

Angel Olazábal, M.D.

**CITOMEGALOVIRUS ASOCIADO A MALFUNCIONAMIENTO DEL SISTEMA INMUNOLÓGICO.**

Ha ocurrido un aumento en la evidencia que asocia la infección por citomegalovirus (CMV) en adultos saludables con la presencia de inmunodeficiencia e infecciones oportunistas y neoplasmas. Los estudios indican que los homosexuales constituyen una gran subpoblación en la cual la incidencia de infección por este virus es de hasta 94%. Estadísticas recientes muestran que las infecciones por el virus Epstein-Barr (EBV), mononucleosis, hepatitis B y por el virus herpes simplex (HSV) también son frecuentemente asociadas con este mismo grupo de personas.

Tres nuevos estudios nos proporcionan evidencia adicional a favor de la hipótesis de que existe una relación directa entre CMV y otras infecciones en hombres homosexuales. Gottlieb y colaboradores describieron los casos de cuatro pacientes homosexuales que desarrollaron pulmonía severa causada por *P. carinii*, además de infección con HSV y Candida. En cada caso se aisló CMV de varias secreciones y había evidencia de infección activa por CMV; en varios casos hubo evidencia de infección previa por CMV mononucleosis. Todos eran anérgicos y significativamente linfopénicos. Los linfocitos de estos pacientes no respondieron a antígenos comunes y

sufrían intercambios marcados en la razón de infocitos supresores sobre linfocitos auxiliares ("helper lymphocytes"). Estos hallazgos inmunológicos son consistentes con CMV.

Masur y asociados evaluaron 11 pacientes con pulmonía producida por *P. carinii*. Todos eran drogadictos (7), homosexuales (6), o ambos (2). La mitad de estos pacientes tenía historial del síndrome pseudo-mononucleosis (mononucleosis-like syndrome) previa a la pulmonía. Uno de ellos desarrolló sarcoma de Kaposi y otro desarrollo linfadenopatía angioinmunoblástica. Los estudios inmunológicos muestran una disminución en la cantidad y en la calidad de función de los linfocitos. Aunque no se realizaron estudios virales definitivos en todos los 11 casos, al menos uno de los pacientes murió por complicación pulmonar con CMV y *P. carinii*.

Siegel y colaboradores estudiaron cuatro homosexuales que desarrollaron infección con HSV con ulceraciones; en tres casos hubo evidencia de coexistencia con infección por CMV. Tres murieron y cuatro desarrollaron sarcoma de Kaposi. Todos los pacientes eran anérgicos a antígenos comunes y además mostraban linfopenia con conteos que no excedían los 1,000. Como en reportes previos, las células T fueron suprimidas y hubo un mayor por ciento de células supresoras a células auxiliares (helper cells); hubo una disminución en la actividad de células asesinas (killer-cell) en contra de HSV. (Gottlieb, M.S., et al: *N. Engl. J. Med.* 305:1425, 1981; Masur, H., et al: *N. Engl. J. Med.* 305: 1431, 1981; Siegal, F.P., et al: *N. Engl. J. Med.* 305:1439, 1981).

**Comentario:** CMV es reconocida como una de las causas de malfuncionamiento del sistema inmunológico, tanto en animales como en el humano y tiene la capacidad de inducir linfopenia y suprimir muchas funciones expresadas por las linfocitos (lymphocyte-expressed functions). CMV se trasmite sexualmente y es transportada en varios fluidos del cuerpo incluyendo el semen. La población de homosexuales parece estar altamente expuesta a este virus. Existe la interrogativa; ¿será CMV sólo el responsable por la inmunosupresión o existirá otro factor común en esta población que esté contribuyendo?

CMV suele estar acompañado de *P. carinii* en infecciones de neonatos y de individuos con inmunosupresión; y existe evidencia de que CMV puede crecer entre organismos de pneumocistis. Estudios *in vitro* con CMV han demostrado que éste es capaz de disminuir varias funciones inmunológicas permitiendo que otros virus y organismos invaden el cultivo. CMV puede ser transportado en el sistema reticuloendotelial por años, donde su influencia a largo plazo ha sido investigada

recientemente en homosexuales con malfuncionamiento del sistema inmunológico.

C.H. Ramírez-Ronda, M.D.

**AN ELECTROMYOGRAPHIC ANALYSIS OF THE EFFECTIVENESS OF HEAT OR COLD AND STRETCHING FOR INDUCING RELAXATION IN INJURED MUSCLE.** Prentice Jr. W.E. *J Orthop, Sport Phys. Ther.* 1982, 3: 133-140.

The study examined the use of heat and cold therapy in conjunction with either static stretching or a technique of proprioceptive neuromuscular facilitation stretching to determine which combination of these treatment techniques would elicit the greatest amount of relaxation in muscle which exhibits delayed, postexercise pain as indicated by changes in levels of electromyographic activity. Results indicated that a strenuous exercise task can produce an increase in electrical activity and is considered to be effective in inducing experimental muscle pain. The use of cold followed by static stretching appeared to be superior to other treatments in reducing delayed muscle pain. Treatments involving the use of cold followed by some type of stretching are more effective than treatments involving heat and stretching for inducing muscle relaxation. Treatments involving static or proprioceptive neuromuscular facilitation stretching appear equally effective in reducing muscle pain; and that subcutaneous fat may serve as a type of insulation against the penetrative effects of heat or cold therapy.

Herman J. Flax, M.D.

**THYMECTOMY FOR MYASTHENIA GRAVIS. A CHANGING PERSPECTIVE.** Heiser J.C. Rutherford R.B. and Ringel S.P. *Arch Surg.* 1982, 117: 533-537.

A review of 28 patients with nonthymomatous myasthenia gravis who underwent thymectomy at the University of Colorado Health Sciences Center, Denver, from 1967 to 1979 shows significant stepwise changes in management and results. Comparison among 3 periods—period 1 (1967-1971), when thymectomy competed with prednisone, which was not given in the perioperative period (7 patients). Period 2 (1974-1976), when thymectomy as followed by 6 months of prednisone therapy (10 patients); and period 3 (1977-1979), when prednisone was also given to prepare the patients for thymectomy (11 patients)—demonstrated a decreasing need for tracheostomy and respiratory support (86, 10 and 0%, respectively), shorter stay in the intensive care unit (21, 3 and 1 day, respectively), and shorter hospitalization (36, 13 and 4 days, respectively). Remission or marked amelioration of symptoms occurred in 56% of group 1 and 100% of both groups 2 and 3. Earlier application of thymectomy and its performance through a short upper transverse incision also contributed to the improved results.

Herman J. Flax, M.D.

**EL ELECTROCARDIOGRAMA EN ESTENOSIS AORTICA:** Fowler RS, Wood MM, Bain H, Patel RG, Sandor G and Rowe R.D. *Pediatric Cardiology* 3:213, 1982.

La determinación directa de la severidad de una estenosis aórtica se obtiene por medio del cateterismo cardíaco. Hay varios métodos indirectos para hacerlo y el electrocardiograma (ECG) de superficie es uno de ellos. En este estudio de la Sección de Cardiología del Toronto Hospital for Sick Children en Canadá se demuestra la utilidad del ECG para determinar dicha severidad.

El estudio comprendió 50 niños con estenosis aórtica en los cuales se comparó el gradiente sistólico a través de la válvula, obtenido en el cateterismo cardíaco, con varios parámetros del ECG. La mejor correlación se obtuvo midiendo la onda T en aVF y  $V_6$ , la onda Q en  $V_6$  y la suma de  $SV_1$  y  $RV_6$ . A mayor gradiente, menor es la amplitud de la onda T en aVF y  $V_6$ ; la onda Q en  $V_6$  se hace también más pequeña y en algunos casos desaparece. Con la aplicación de una fórmula a estos valores puede determinarse el gradiente con bastante precisión ( $r=6.36$ ) y a su vez es muy útil para el seguimiento del paciente. Según los autores en el seguimiento del paciente un aumento mayor de 50mm Hg en el gradiente estimado utilizando esta fórmula es indicación para un estudio hemodinámico invasivo. Si la T en aVF es  $\leq 0.1$ mv, o la T en  $V_6$  es  $\leq 0.3$  MV, o la Q en  $V_6$  está ausente debe hacerse el cateterismo cardíaco.

Rafael Villavicencio, M.D.

**SMALLPOX EPIDEMICS IN PUERTO RICO DURING THE PRE VACCINE ERA (1518-1803).** Rigau Pérez JG. *Journal of the History of Medicine and Allied Sciences* 37: 423-438, 1982.

La primera epidemia de viruela en América, en 1518, introdujo la enfermedad en Puerto Rico, donde causó la muerte de dos terceras partes de la población taína. Con la epidemia siguiente (1689-90) enfermó más de la mitad y murió el 27% de la población de San Juan. El principal promotor de la viruela fue el tráfico de esclavos. La introducción de esclavos de Africa trajo la enfermedad a América, contribuyendo grandemente a la extinción de los indios. Esto motivó la importación de más esclavos, lo cual a su vez introdujo repetidamente la infección en Puerto Rico hasta que la viruela cobró carácter endémico y se convirtió en amenaza para toda la población. Las medidas preventivas utilizadas tradicionalmente por los moradores de la capital se vieron desafiadas en la epidemia de 1792-93 por el uso de la inoculación (variolización). Esta fue la primera discusión pública de un asunto científico en Puerto Rico, reflejo de la complejidad de actitudes y potencialidades en la sociedad del momento. Estas circunstancias propiciaron la utilización exitosa de la vacuna jenneneriana en 1803, con anticipación a las otras colonias españolas de América.

José G. Rigau, M.D.





## IMPLICACIONES FINANCIERAS DE SALUD PARA TODOS



El costo para que todos los ciudadanos de las Américas logren acceso a los servicios de salud se incrementará de 32 billones de dólares anuales en 1980 a 60 billones de dólares anuales en el año 2000, de acuerdo a un documento de información sobre las implicaciones del Plan de Acción de Salud para Todos presentado durante la 21a Conferencia Sanitaria Panamericana.

El Plan de Acción destaca procedimientos para extender acceso a los servicios de salud a los 120 millones de ciudadanos de América Latina y el Caribe que en la actualidad no cuentan con ellos.

Los costos actuales para salud en las Américas se estiman alrededor de 32 billones de dólares anuales provenientes de diferentes fuentes abarcando tanto la inversión del capital como los costos de operación de atención de salud, o cinco por ciento del Producto Nacional Bruto (PNB) de la Región.

Se estima que a partir de la fecha hasta el año 2000, la inversión de capital para agua potable, saneamiento, y servicios de salud será de alrededor de 178 billones de dólares.

Se espera que estas inversiones generen en el año 2000 costos de operación anuales periódicos de 18,75 billones de dólares para atención de salud y 17,6 billones de dólares para agua y saneamiento, de los cuales 11,6 billones de dólares serán indemnizados por medio de honorarios del usuario.

Las proyecciones macroeconómicas "ofrecen expectativas razonables de que la mayoría de estos países de la Región dispondrán de recursos suficientes para equiparar dichos costos," anota el documento, incluso con un estimado bajo de cuatro por ciento anual del crecimiento económico y cuatro por ciento del PNB consignado a la salud.

## ABUSO DE DROGAS PROBLEMA SERIO EN LAS AMERICAS

El abuso de drogas es un serio problema de salud pública y social en las Américas, y es necesario establecer programas adicionales de control y tratamiento para combatirlo, de acuerdo a un informe presentado a la Conferencia Sanitaria Panamericana.

El documento que cita datos de varias investigaciones,

anota que el abuso de drogas está diseminado ampliamente en la mayoría de las poblaciones estudiadas, contándose con marihuana, sedativos, hipnóticos, amfetaminas, pasta de cocaína, e inhalantes, como las principales drogas de abuso.

El índice de edad de la población afectada es muy extenso e incluye un vasto porcentaje de adultos, especialmente mujeres. Asimismo es evidente, según los datos de jóvenes entre los 13 y 19 años, que el abuso de drogas podría comenzar desde las edades de siete u ocho años.

Hace notar que la prevención efectiva requiere la reducción de la demanda y la disponibilidad de drogas psicoactivas y narcóticas, y el reconocimiento que deberá darse al papel importante que ocupan las autoridades que regulan el uso de drogas y la profesión médica. Se necesitan también enfoques innovativos para ayudar a combatir el abuso de drogas por medio de administración y regulaciones adecuadas de programas de tratamiento en base a la comunidad.

La Organización, en colaboración con el Fondo de las Naciones Unidas para el Control de Abuso de Drogas, está involucrada en varios proyectos regionales y de país sobre drogas y está buscando fondos extrapresupuestarios para proyectos adicionales.

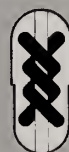
## SE PIDE PRIORIDAD PARA INVESTIGACION DE INFECCIONES RESPIRATORIAS AGUDAS

El Comité Asesor sobre Investigaciones Médicas de la OPS ha recomendado dar alta prioridad a la investigación sobre infecciones respiratorias agudas, que consumen una proporción considerable de los recursos sanitarios de la Región.

También recomendó la integración de la investigación y las medidas tomadas para reducir la morbilidad y la mortalidad en los niños menores de cinco años.

El Comité, integrado por distinguidos científicos de todo el continente americano, asesora al Director de la OPS. Sus recomendaciones fueron presentadas en la XXI Reunión Cuadrienal de la Conferencia Sanitaria Panamericana.

El Comité recomendó que se amplíen los esfuerzos de la OPS relacionados con la investigación de los servicios sanitarios, y que se difunda la información sobre la actual investigación, así como sobre la investigación permanente acerca de nutrición, salud mental, salud de los ancianos, enfermedades crónicas cardiovasculares, salud ambiental, enfermedades tropicales y desarrollo cerebral y mental.



## NATIONAL COUNCIL ON DRUGS

### RELATIVE EFFICACY AND SAFETY

The National Council on Drugs believes that the decision on the availability of drugs based on *relative* efficacy and safety should not be made solely by the Food and Drug

Administration. Further, the NCD feels that the decision regarding which drug to use for an individual patient should be made by the physician and the patient.

The ultimate end of unbridled regulation by the FDA could result in only one approved drug being available in each therapeutic class. If one were to make a list of drugs in each category and compare their relative efficacy and relative safety, one would end up with a single drug as the drug of choice in each category of compounds and all other drugs would be measured according to that standard. A new drug in that category could not be introduced unless it had superior efficacy or greater safety; then it would become the drug of choice. This could create problems for the practicing physician because anyone who has practiced medicine knows that a patient may tolerate one drug better than they do another. Therefore, the physician must have some alternative therapeutic choices.

There is evidence in recent years of FDA attempts to make that choice for the physician by removing drugs from the market that government regulators consider either more toxic or less effective than other drugs in a given class. The NCD feels that this is an encroachment on the free choice of the physician that is not warranted or allowable by statute. It is well within the scope of the FDA to label drugs appropriately. If one drug in a category has an adverse reaction that another one does not, that could be stated in the labeling, but the FDA does not have the right to remove the drug from the market unless it is an imminent hazard, in that serious and life-threatening side effects are associated with its use.

After the appropriate evaluation of each drug has been made and the proper labeling with allowable indications and appropriate warnings are established, the physician should be free to decide on whether to prescribe the drug or not.

## DRUG REGULATION VS. FREEDOM OF CHOICE

Regulation of drug research and availability necessarily entails some restriction on the access of patients and their physicians to any therapy they might choose. Seeking a balance between an individual's freedom of choice and society's need to ensure that the drugs available have been proven safe and effective requires difficult judgmental choices on the part of policy-makers. In recent years, issues have arisen in which it is claimed that present U.S. policies are too strict and that patients should have the right to use untested remedies as therapies.

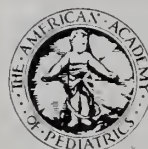
The National Council on Drugs is in complete agreement with the relevant parts of the existing law and the policy of the Food and Drug Administration: that efficient development and utilization of drugs for human use should be based on careful comprehensive, and reproducible research by qualified investigators who have used in vitro studies, appropriate animal models, and carefully controlled clinical trials. Only rare exceptions should be made to permit the clinical testing of substances that have been shown to produce, at best, equivocal effects in pre-clinical studies.

On the other hand, the NCD is convinced that many therapeutic advances have been achieved through serendipity and that overemphasis on "approved" uses of specific drugs

may stifle meritorious clinical investigation. This is particularly true when drugs have had a long and unchallenged record of therapeutic efficacy in other countries.

The NCD is firmly opposed to quackery of any sort. Yet it strongly supports careful scientific inquiry into enlightened but "unapproved" uses of a drug. Typically the former is characterized by testimonial advocacy, whereas the latter is characterized by prospective studies and other appropriate experimental designs are all freely submitted to critical review prior to publication, regardless of whether or not the original hypothesis is vindicated.

In summation, the NCD supports the right of investigators to investigate any possible use of any drug, with a minimum of regulatory interference, provided that the investigation is recognized as such and that truly informed consent is obtained from all experimental subjects.



## STUDY SUGGESTS USING ANESTHESIA FOR CIRCUMCISION

An anesthetic which is simple to use and usually causes no complications should be considered for every infant who undergoes circumcision, says an article published in the January issue of *Pediatrics*, the journal of the American Academy of Pediatrics.

The article reports results of a study conducted to determine how newborn males respond to the dorsal penile nerve block, which was developed in 1978 by Kirya and Werthmann as a local anesthetic for use during circumcisions. The new study was conducted by Paul S. Williamson, M.D., and Marvel L. Williamson, R.N., at the University of Iowa Hospitals and Clinics in Iowa City.

While many parents wrongly assume that their baby boys are anesthetized during the operation, the researchers described the contrasting behavior of and stress measurements on babies who are and are not numbed to the pain caused by the procedure.

The Williamsons point out that some physicians believe anesthesia is not needed during circumcision because it is a relatively brief procedure and others think newborns do not feel pain during circumcision because their nerves do not have the sheathing which helps to transmit painful stimuli. The new study's results contradict both these assumptions.

A total of 30 healthy newborns were circumcised for the study. Twenty were anesthetized for the surgery, and a matched control group of 10 newborns were circumcised without anesthesia. The infants' heart rates, time spent crying, and oxygen levels (previously found to drop with infant pain) were monitored before, during and after the operation. The three kinds of measurements were taken to determine how much stress the infants were undergoing. Results of the study showed that for all three measurements, the infants who received anesthesia experienced significantly less stress.

"Although infants cannot verbally describe pain," say the Williamsons, "the experience may have profound physiologic and psychological effects." The researchers also point out that sick or premature infants, who must endure other painful unanesthetized procedures, may undergo physiologic changes which are "clinically significant".



## PACIFIERS HELP PREEMIES GROW FASTER, STUDY SHOWS

Giving premature infants pacifiers to suck during tube feedings may help them gain weight faster and lead to shorter hospital stays, according to a newly published study.

The study is published in the January issue of *Pediatrics*, Journal of the American Academy of Pediatrics. It was conducted at the Children's Hospital of Philadelphia by a team of physicians headed by Judy C. Bernbaum, M.D., FAAP.

The study was done to determine whether pacifiers would help premature infants develop the sucking reflex, an important factor in whether the babies can be fed orally and in improving their nutrition and maturation. Few infants have fully developed sucking behavior at younger than 24 weeks of gestation, and premature infants are routinely fed through tubes, a method known as gavage feeding.

A total of 30 medically stable premature infants were studied. Fifteen who were given pacifiers during gavage feedings were matched with 15 infants of similar birth weight and age who were not given the pacifiers. The average gestational age for the infants was 31 1/2 weeks at the beginning of the study.

The researchers found that infants given the pacifiers did develop a sucking reflex more quickly than infants who did not. The differences between the two groups first appeared at 34 weeks of gestation. Infants using pacifiers sucked more often with each "burst" (three or more uninterrupted sucks) and their sucking was also less sporadic than infants not given pacifiers.

One result which the researchers had not expected to find was that the infants using pacifiers gained weight more quickly than those who did not, in spite of the fact that both groups took in the same number of calories. The mean average weight gain for infants using pacifiers was 180 grams per week compared to 120 grams per week for those not given pacifiers. The reasons for the greater weight gain are unclear but the researchers speculate that the infants using pacifiers may have been less restless and therefore used less energy, or that they absorbed nutrients more efficiently.

The researchers also found that the gastrointestinal systems of the infants using pacifiers were more efficient, and that the infants made the transition to oral feedings more quickly. Infants who used pacifiers also reached the weight at which they could be released from the hospital, two kilograms, six days earlier than those who were not given pacifiers, and the average length of hospital stay was seven days shorter for the group using pacifiers.



## Lung cancer is now an equal opportunity tragedy.

Remember when lung cancer was a man's disease. Because men had been smoking longer than women. But the women's smoking boom that started in the 1930's and 40's—is paying most cruel dividends today. Yet most people still think lung cancer is a man's disease. Tell your female patients the true story. That lung cancer is now an equal opportunity tragedy. That's what "you've come a long way, baby" is all about.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
Office on Smoking and Health  
Public Health Service Rockville, MD 28057



## EXERCISE MAY PROTECT AGAINST SOME HEART ATTACKS

People who make vigorous exercise a habit may be protected against heart attacks.

This is not the first time for such a suggestion. But David S. Siscovik, MD, and colleagues at the University of Washington in Seattle, have statistical evidence to back it up.

They found that people who engage often in "high-intensity leisure time activity", such as jogging, swimming, singles' tennis and squash, have a reduced risk of primary cardiac arrest. In the Dec. 17 issue of *Journal of the American Medical Association*, they define primary cardiac arrest as a heart attack due solely to heart disease and no to other causes such as injury, drug overdose or respiratory failure.

Siscovik, who is now with the University of North Carolina, Chapel Hill, studied 163 married men aged 25 to 75 years who had suffered primary cardiac arrest and a control group whose members were free of heart disease. He questioned the wives of both the patients and the control subjects about the types and frequency of exercise in which their husbands engaged and estimated the amount of energy the men expended. A significantly higher number of patients than controls fell into a low exercise category (less than 20 minutes per week).

Because the study considered only one year of exercise prior to the heart attack, the researchers could not determine whether the apparently reduced risk of primary cardiac arrest was the result of long-term or relatively short-term participation in vigorous exercise. Siscovik said it is unclear whether a person who begins to engage in vigorous exercise late in life would achieve protection from primary cardiac arrest.

Many questions about the role of physical activity in cardiovascular disease remain unanswered, writes cardiovascular disease specialist William B. Kannel, MD, of Boston University Medical Center, in an accompanying editorial. The amount of exercise needed to achieve benefits and the duration of the benefits is uncertain. It is possible that physical activity affects peripheral areas of the circulation more than the heart. An many researchers disagree about how much benefit is the result of physical activity and how much the result of changes in other risk factors, such as an overly rich diet and smoking.

"Physical exercise is best prescribed as one component of a comprehensive program for avoiding coronary heart disease,"

Kannel advises. "While sustained regular exercise at 50 percent to 75 percent capacity for 15 to 30 minutes at least every other day is required to maintain a training effect, there is some evidence that lesser levels of exercise may also be beneficial. A vigorous walking program may be more prudent for middle-aged flabby, deconditioned Americans. This will also minimize the considerable orthopedic side effects of strenuous exercise, e.g., jogging," Kannel says.

## BENEFITS AND HAZARDS OF RUNNING

Runners who increase their weekly mileage in search of greater health benefits may also increase their chance of injury, according to a report in the Dec. 17 *Journal of the American Medical Association*.

Jeffrey P. Koplan, MD, and colleagues at the Centers for Disease Control (CDC) in Atlanta, with the help of the Georgia Department of Human Resources, surveyed 1,423 of the 25,000 registrants of the July 4, 1980, Peachtree Road Race, Atlanta's annual 6.2 mile run. The questionnaire included running habits, injuries experienced, hazards encountered, and changes in smoking and weight status for the period July 4, 1980, to July 3, 1981.

According to Koplan, CDC's assistant director for public health practice, 89 percent of male runners and 69 percent of female runners still ran regularly one year after the race; 81 percent of male runners and 75 percent of female runners who were smokers when they began running had quit; and 38 percent of male runners and 16 percent of female runners had lost more than 10 pounds.

But hazards accompanied these benefits, Koplan says. Thirty-five percent of all runners surveyed suffered musculoskeletal injuries serious enough to require a decrease in weekly mileage. Knee injuries were most frequent. The risk of injury increased in proportion to mileage, Koplan reports.

After injuries, runners were most in danger of being hit by thrown objects, including cans, bottles, ice, liquids and, in one case, a bag filled with rocks. Other hazards, in descending order of occurrence, included being bitten by dogs, hit by bicycles and struck by motor vehicles.

"Runners should consider the tradeoffs inherent in increasing or decreasing their weekly mileage", writes Koplan.

## AVOIDING STRESS AND CERTAIN FOODS MAY RELIEVE SYMPTOMS OF CORONARY ARTERY DISEASE

Additional evidence that patients with coronary artery disease can help themselves by altering their lifestyles comes from



a group of Houston researchers writing in the *Journal of the American Medical Association*, January 7, 1983.

A team headed by Dean Ornish, MD, who is now with Massachusetts General Hospital and Harvard Medical School, Boston, helped a small group of patients improve their capacity for exercise and reduce the frequency of chest pain with a program combining a strict vegetarian diet and stress management techniques.

Ornish's group studied 46 patients aged 45 to 75 years who had medically diagnosed coronary artery disease. They were divided randomly into a control group who continued their routine activities at work and home and an experimental group that began a 24-day intervention program.

Those in the experimental group were housed together in a rural environment where they learned stress management techniques and consumed a nutritionally balanced diet essentially devoid of animal products, salt, sugar, alcohol and caffeine. The stress management techniques included stretching and relaxation exercises, yoga-like meditation and visualization methods in which the patients imagined themselves free of disease.

Both groups underwent exercise tests and plasma cholesterol determinations and were questioned about medication usage and frequency of attacks of anginal chest pain.

At the end of the intervention period, the experimental group could exercise 44 percent longer and showed a 20.5 percent reduction in plasma cholesterol levels. Their angina attacks decreased from about ten per week to about one or two. Laboratory tests also showed an improvement in heart muscle function. Eight patients were able to discontinue anti-hypertensive medication and ten others reduced their dosages. No such changes occurred in the control group.

Ornish speculates that the dietary changes and stress management techniques may have caused the improvements in the experimental group by initiating metabolic changes that reduce the likelihood of coronary artery spasm and formation of atherosclerotic plaques.

"Interpretation of these findings must be tempered with caution," he warns, "since the patient population is selected and the sample size is relatively small." The controlled residential environment in which the experimental group lived may have contributed to the measured improvements, and it remains to be proved whether the high level of compliance they achieved could be obtained with patients managed on an outpatient basis, Ornish says.

Still he indicates, the intervention produced results, and it is safe and compatible with conventional treatments of coronary artery disease.

**DAY-CARE CENTERS IMPLICATED  
IN DISEASE OUTBREAKS**

Infections contracted at day-care centers have been traced as the source of outbreaks of illness in numerous communities, according to a January issue of the *Journal of the American Medical Association*.

The outbreaks include epidemic jaundice from hepatitis A, dysentery and other diseases spread by organisms that can

thrive in the intestines.

Although no comprehensive figures are known for the number of communities involved or the number of cases directly linked to day-care centers, the situation, according to Stanley H. Schuman, MD, at the Medical University of South Carolina in Charleston, is "reminiscent of the presanitation days of the 17th century".

Writing in an editorial in *JAMA*, Schuman said that a child runs a 25 percent risk of suffering a disease that leads to diarrhea during the first five weeks of enrollment in a day-care center. Disease organisms that cause either no symptoms or diarrhea in preschool children can spread to adults and have more severe consequences.

More than 11 million youngsters are in day-care, according to figures from the United States Department of Health and Human Services. Of these, Schuman notes, some 5 million go to private homes served by a nonrelative, 4 million are served at their own homes by a relative or nonrelative, and nearly 2 million attend organized small and large day-care centers.

The day-care setting is conducive to transmission of disease because, Schuman said, day-care proprietors have little training for food handling, yet they serve more meals and snacks than many restaurants. Children enter and leave in an erratic pattern, ensuring maximum mixing of infected susceptible subjects. Infants and toddlers in diapers can be a source of intestinal germs transmitted from soiled diapers.

Toddlers, Schuman said, have been clocked at putting a hand or object in the mouth every three minutes. He also said that day-care personnel develop a "casual, tolerant attitude toward frequent lapses in sanitary routines".

The lead article in the same issue of *JAMA* recounts the experience of health officials in Phoenix, Arizona, in stemming an epidemic of hepatitis A in Maricopa County by giving injections of immunoglobulin to all day-care center children and employees whenever hepatitis occurred in 91 of the country's day-care facilities.

Immunoglobulin contains antibodies against a number of diseases including hepatitis A, and has been proven effective in the past in stopping the spread of hepatitis.

In the 12 months prior to the immunoglobulin trial, which took place from October 1979 to June 1981, there were 225 new hepatitis cases a month on average in children and adults in the county. The number of cases fell to an average of 52 per month during the final nine months of the trial, according to Stephen C. Hadler, MD, of the Centers for Disease Control in Phoenix.

Hadler, the primary author of the *JAMA* study, said the decrease occurred not only in children in day-care centers and their families, but also in people not directly associated with the centers, probably because of decreased spread from day-care families into the community at large.

Although the immunoglobulin trial, waged against hepatitis associated with day-care centers, had a dramatic impact on the level of hepatitis in the general community, the outcome for other illnesses known to occur in day-care centers is not so promising, Schuman said.

Little immunity occurs for many infections that cause gastrointestinal disease in children. Aside from rigorous hand washing to combat the illnesses that can cause diarrhea, Schuman suggests that day-care personnel be educated in the basics of food handling and that physicians as a group assist day-care operators in improving health standards.

## MEASLES ON WAY OUT IN U.S. BUT CAUTION URGED

The dramatic decrease in measles cases over the past two decades in the United States is no reason for relaxing efforts to have all children immunized, according to Edward N. Brandt, Jr., MD, assistant secretary for health, Department of Health and Human Services.

The nation's goal of eliminating measles as an indigenous disease by the year's end is likely to be reached, Brandt says, but the achievement cannot be made permanent without continued support for immunization and reporting programs.

In a letter to the editor in the *Journal of the American Association*, Brandt reports that the incidence of this once common childhood disease has decreased from 500,000 cases annually 20 years ago to just more than 3,000 cases in 1981. Only 1,090 cases were reported in the United States in the first 30 weeks of 1982.

But, warns Brandt, physicians and other health care providers must continue to educate parents about the importance of complete immunizations for their children and must report suspected cases of measles immediately to their local health departments for investigation and follow-up.

"The cost of disease prevention is but a fraction of the cost of care once a disease has occurred," Brandt writes. "The savings that accrue when a disease is prevented are measured not only in dollars but in the time, effort, suffering and loss of life," he adds.

"We are on the verge of conquering measles," according to Brandt. "We can make measles a memory for future generations."

## AIDS VICTIMS FOUND AT RISK FOR RARE BACTERIAL INFECTION

Eight of nine patients who died with acquired immunodeficiency syndrome (AIDS) at a University of California hospital were found to have disseminated infections with a bacterial strain that rarely causes disease in healthy people.

Writing in a December issue of the *Journal of the American Medical Association*, Phillip Zakowski, MD, and colleagues from the UCLA Center for the Health Sciences, Los Angeles, report the cases of five of those AIDS patients, homosexual males, who died with disseminated infections with *Mycobacterium avium-intracellulare*, a strain that is common in the environment but only seldom causes disease in humans. When it does strike, the result is most often localized lung disease.

AIDS has been reported recently in persons who are homosexuals and/or intravenous drug abusers. It is characterized by alterations in the patient's immune system that put him at risk for a variety of infections and for a tumor known as Kaposi's sarcoma.

Because Zakowski's patients suffered from a number of infections, it is unclear what role the mycobacterial infection

played in their altered immunity and subsequent deaths. Although Zakowski and his group consider their findings preliminary, they suggest that doctors seek evidence of mycobacterial infection in homosexuals with signs of AIDS.

In an accompanying editorial, however, Henry Masur, MD, of the National Institutes of Health, Bethesda, MD., writes that prompt diagnosis of mycobacterial infection has rarely helped AIDS patients because the organisms are almost always resistant to most antimycobacterial drugs. Most patients have died, despite treatment with multiple-drug regimens.

Since AIDS patients are susceptible to such a wide range of devastating infections and cancers, Masur advises that real progress in treating this condition will be made by discovering how AIDS is transmitted and how it alters the body's immune defenses.



"Give me  
one good reason  
to stop smoking."

Your baby.







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**A.P.G.U.E.**

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**SAN JUAN, PUERTO RICO  
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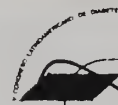


The Graduate School of Public Health, San Diego State University, San Diego, California, is now accepting applications from obstetricians, pediatricians, and other physicians interested in a career in the field 1983. The Training Program is of nine months duration. The **Master of Public Health** degree is awarded. Considerable effort is made by the Faculty to assist each student in career planning.

There is also available a special 21-month Training Program for pediatricians in the field of **Handicapped Children**.

Inquiries should be addressed to:

Helen M. Wallace, M.D.  
Professor and Head  
Division of Maternal and Child Health  
Graduate School of Public Health  
San Diego State University  
San Diego, CA 92182



**ASOCIACION LATINOAMERICANA DE DIABETES  
V CONGRESO LATINOAMERICANO  
DE DIABETES**

**4 a 8 Abril de 1983, Santiago, Chile  
Secretaría General, Chacabuco 419, 2do. Piso, Santiago,  
Chile**

La Asociación Latinoamericana de Diabetes eligió a la ciudad de Santiago de Chile como sede del V Congreso Latinoamericano de Diabetes, evento a desarrollarse entre el 4 y 8 de Abril de 1983.

El Comité Directivo del Congreso al tomar esta responsabilidad, se fijó como objetivo organizar un torneo que logre no sólo excelencia científica, sino que sea motivo de unión y amistad entre todos los profesionales médicos y de colaboración médica que trabajan en Latinoamérica en el campo de la diabetes.

Con este doble espíritu invitan a concurrir a la cita de Santiago de Chile, a fin de alcanzar el éxito que la diabetología latinoamericana se merece. El brillo del V Congreso Latinoamericano no dependerá de este Comité Directivo, que es sólo un intermediario, sino del apoyo generoso que Uds. le brinden con su asistencia.

## MEETINGS IN THE UNITED STATES

April 1983

American Association of **Neurological Surgeons**, Sheraton-Washington, *Washington, DC*, April 24-28. Exec. Dir: C.H. Hauber, CAE, 625 N Michigan Ave, Suite 1519, Chicago, IL 60611.

American College of **Nuclear Medicine**, Amfac Hotel, *Dallas*, April 29-May 1. Pres: R.L. Bell, MD, PO Box 198, Downingtown, PA 19335.

American Federation for **Clinical Research**, Sheraton, *Washington, DC*, April 29-May 2. Info: C.B. Slack, 6900 Grove Rd, Thorofare, NY 08086.

American **Fertility Society**, San Francisco Hilton, *San Francisco*, April 19-20. Med Dir: H.H. Thomas, MD, 1608 13th Ave South, Suite 101, Birmingham, AL 35256.

American **Laringological, Rhinological, and Otological Society**, Fairmont, *New Orleans*, April 12-14. Info: W. Tribble, MD, 2954 Dorman Rd, Broomall, PA 19008.

American Medical Society on **Alcoholism**, Hyatt Regency, *Houston*, April 14-20. Sec: J.G. Chen See, MD, AMSA, 733 3rd Ave, New York, NY 10017.

American **Occupational Medical Association**, Washington Hilton, *Washington, DC*, April 24-29. Info: D. Hogan, PhD, 150 Wacker, Chicago, IL 60606.

American **Otological Society**, Fairmont Hotel, *New Orleans*, April 10-11. Sec-Treas: D.T. Cody, MD, Mayo Clinic, Rochester, MN 55901.

American **Physiological Society**, *Chicago*, April 10-15. Info: O.E. Reynolds, MD, 9650 Rockville Pike, Bethesda, MD 20014.

American **Radium Society**, Hyatt Regency, *Savannah, Ga*, April 5-9. Exec Sec: S.R. Polek, Office of the Secretariat, American Radium Society, 925 Chestnut St, Philadelphia, PA 19107.

American **Roentgen Ray Society**, Atlanta Hilton, *Atlanta*, April 18-22. Sec: R.A. Gagliardi, MD, Suite 105, 880 Woodward Ave, Pontiac, MI 48053.

American Society for **Adolescent Psychiatry**, Barbizon-Plaza, *New York*, April 29-May 1. Exec Sec: M.D. Staples, 24 Green Valley Rd, Wallingford, PA 19086.

American Society for **Clinical Investigation**, Sheraton Washington, *Washington, DC*, April 29-May 2. Sec-Treas: M.M. Frank, MD, National Institutes of Health, Bldg 10, RM 11N228, Bethesda, MD 20205.

American Society for **Clinical Nutrition**, Sheraton Washington, *Washington, DC*, April 21-23. Info: V. Coates, 765 Commonwealth Ave, Boston, MA 02215.

American **Urological Association**, Las Vegas Hilton Hotel, *Las Vegas*, April 17-21. Exec Sec: R.J. Hannigan, 1120 N Charles St, Baltimore, MD 21201.

Society of **Cardiovascular Anesthesiologists**, Sheraton, *San Diego*, April 24-27. Exec Sec: J.A. Hinckley, PO Box 11083, Richmond, VA 23230.

Society for **Pediatric Radiology**, Hyatt Regency, *Atlanta*, April 15-17. Sec: B.P. Wood, MD, PO Box 648, 601 Elmwood Ave, Rochester, NY 14642.

May 1983

American **Cancer Society, Breast Cancer**, Sheraton Boston Hotel, *Boston*, May 19-21. Info: American Cancer Society, 777 3rd Ave, New York, NY 10017.

American **Cleft Palate Association**, Hyatt Regency, *Indianapolis*, May 4-7. Admn Sec: J.A. Graminski, 331 Salk Hall, Univ of Pittsburgh, Pittsburgh, PA 15261.

American College of **Obstetricians and Gynecologists**, Atlanta Hilton, *Atlanta*, May 8-12. Exec Dir: W.H. Pearse, MD, 600 Maryland Ave, SW Washington, DC 20024.

American College of **Sports Medicine**, Town & Country Hotel, *San Diego*, May 23-26. Exec Dir: T. Miller, American College of Sports Medicine, 1440 Monroe St, Madison WI 53706.

American **Geriatrics Society**, Roosevelt, *New York*, May 12-13. Exec Dir: K. Henderson, c/o AGS, 10 Columbus Circle, New York, NY 10019.

American **Lung Association**, Radisson-Muehlebach, *Kansas City, Mo*, May 8-11. Dir: J.A. Swomley, 1740 Broadway, New York, NY 10019.

American **Orthopaedic Association**, sponsored by Campbell Foundation Univ of Tennessee, and Orthopaedic Surgery Residency Program, Holiday Inn Rivermont, *Memphis*, May 11-14. Info: R. Holcomb, MD, Campbell Clinic, 869 Madison Ave, Memphis, TN 38104.

American **Pediatric Society**, Hilton Sheraton, *Washington, DC*, May 3-6. Info: D. Goldring, MD, PO Box 14871, St Louis, MO 63178.

American **Psychiatric Association**, *New York City*, May 2-6. Dir: M. Sabshin, MD, 1400 K St, NW, Washington, DC 20006.

American Society for **Gastrointestinal Endoscopy**, Washington Hilton, *Washington, DC*, May 21-27. Exec Dir: W.T. Maloney, 13 Elm St, Manchester, MA 01944.

American **Thoracic Society**, Radisson-Muehlebach, *Kansas City, Mo*, May 8-11. Exec Dir: S.R. Iannotta, 1740 Broadway, New York, NY 10019.



American **Surgical** Association, Boca Raton Hotel & Club, *Boca Raton*, Fla, May 12-14. Sec: W.G. Austen, MD, Dept of Surgery, Massachusetts General Hospital, Boston, MA 02114.

American **Trauma** Society, *Chicago*, May 5-6. Exec Dir: B.D. Sutton, Suite 3010, 875 N Michigan Ave, Chicago, IL 60611.

**Neurosurgical** Society of America, Key Biscayne Hotel, *Key Biscayne*, Fla, May 8-11. Sec: J.L. Story, MD, 7703 Floyd Curl Dr, San Antonio, TX 78284.

Society for **Pediatric Research**, Sheraton, *Washington, DC*, May 3-6. Sec-Treas: W. Berman, Jr, MD, Pediatrics, UNM School of Med, Albuquerque, NM 87131.

Society for **Surgery of the Alimentary Tract**, Washington-Sheraton, *Washington, DC*, May 24-25. Sec: R.K. Tomplins, Dept of Surgery, UCLA, Center for the Health Sciences, Los Angeles, CA 90024.

June

American **Diabetes** Association, Hyatt Regency, *San Antonio*, Tex, June 9-14. Exec Vice-Pres: R.S. Bolan, PhD, 2 Park Ave, New York, NY 10016.

American **Medical Electroencephalographic** Association, Hyatt Orlando, *Orlando*, Fla, June 9-12. Exec Dir: R.H. Herzog, 850 Elm Grove RD, Elm Grove, WI 53122.

American Society of **Colon & Rectal Surgeons**, Sheraton Boston Hotel, *Boston*, June 5-9. Admn Sec: H. Gibson, 615 Griswold, no. 516, Detroit, MI 48226.

American Society of **Neuroradiology**, St Francis, *San Francisco*, June 2-4. Dir: R. Perkins, MD, Project HEAR, 1801 Page Mill Rd, Palo Alto, CA 94304.

**Endocrine** Society (65th), Convention Center, *San Antonio*, Tex, June 8-10. Exec Sec: N.C. Karpin, 9650 Rockville Pike, Rockville, MD 20814.

**Flying Physicians** Association, Jackson Lake Lodge, *Moran*, Wyo, June 19-24. Info: A. Cariere, 801 Green Bay Rd, Lake Bluff, IL 60044.

Society of **Nuclear Medicine**, Cervantes Convention Center, *St Louis*, June 7-10. Exec Dir: H.L. Ernstthal, CAE, 475 Park Ave South, New York, NY 10016.

Society for **Vascular Surgery**, Mark Hopkins Hotel, *San Francisco*, June 17-18. Sec: W.S. Moore, MD, Dept of Surgery, UCLA School of Med, Center for Health Science, Los Angeles, CA 90024.

DOUBLE STANDARDS IN THE U.S.

By: John M. Corboy, MD, in the *Hawaii Medical Journal*:

If every family were to go out tomorrow and purchase a \$10,000 new American car, this huge elective expenditure would be lauded as a patriotic rejuvenation of the crumbling auto industry. On the other hand, were every family to go out tomorrow and purchase a \$1,000 appendectomy, this vastly smaller life-saving expenditure would be condemned as further evidence of inflationary escalation in the cost of medical care.

If a million families would build new homes this year, the spectacular investment would be cheered as the salvation of construction and realty industries, but if a thousand lives are saved in expensive critical care units, society laments oppressive medical care costs. We spend more in restaurants than physicians' offices, but there's no call for a "cap" on dining out.

There is a persisting delusion that, while an expenditure for cars and houses is "good" money that cycles quickly through the economy to benefit society on many levels, payment for medical care is somehow "bad" money that completely disappears from circulation, forever lost to productive recycling.

Somehow, it's socially good to spend, even squander, money for things we need but don't want. We happily spend more than 20% of our gross national product (GNP) on leisure goods and services (and are urged to spend more) while we pay less than 14% of our GNP for health care of all types, and it's called a "crisis". Certificates of need are required for CT scanners, but not for Cadillacs.

A ball player or entertainer makes a million dollars, and we agree he's either talented or a good businessman. A surgeon makes \$100,000 and somehow he's a little reprehensible, profiteering off the sick.

**WHILE 85%** of the nation carries health insurance, and thus avoids most of the burden of medical expenses, critics see this not as a prepaid capitalist marvel, but rather as some kind of evil scheme to conceal what apparently should be a painful "awareness of true costs".

The planners all wail the world's greatest medical care system has no incentive to provide cut-rate care, but we all know that cost cutting is furthest from the mind of a sick person. Only the well lament others' medical bills; "unnecessary" surgery is surgery on someone else.

When I think about it, it seems that all of society's attitudes about medical care are paradoxical and contradicting; it's almost a kind of national schizophrenia.

# HOW THE MELTONS FOUND A CURE FOR MEDICAL SCHOOL COSTS.

## Medical School Costs Are Going Up Each Year

While attending Tulane University, Ken and Gwenesta Melton decided to take advantage of the Health Profession Scholarship Program (HPSP) offered by the Army. They are now finishing their Graduate Medical Education in the Army.

**Ken:** I've recommended HPSP to my friends. They worry a little about the military side of it. In no way, I've told them, does the military aspect interfere with the educational process.

**Gwenesta:** Army medicine is very human. You don't have to fill out a million forms, or worry about seeing a certain number of patients for profit reasons.

**Ken:** After you've been in the HPSP a while, the Army offers you an option to spend your six weeks active duty at an Army Medical Center of your choice, anywhere in the country. You make three selections. I didn't get my first choice, but what I did get wasn't too bad. Tripler Medical Center in Hawaii.

---

The Army Medical Department offers an opportunity for financial support for individuals accepted to AMA or AOA accredited medical schools. Approximately 250 students starting their professional education in 1983 will be selected to participate in the Army's Health Professions Scholarship Program (HPSP). The HPSP pays for the participant's tuition, books, instruments (under \$200/item) and, most academic fees required by the school while providing a monthly stipend of \$556 for 10½ months plus active-duty pay for six weeks each year.

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If you are a pre-med student and would like more information on the Health Professions Scholarship Program write or call collect:

AMEDD Personnel Counselor  
DuPont Plaza Office Building  
Room 711  
300 Biscayne Boulevard Way  
Miami, FL 33131  
(305) 358-6489



# 1er CONGRESO PUERTORRIQUEÑO DE CARDIOLOGIA



San Juan , 7 al 10 de abril de 1983.

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Con sumo placer queremos anunciar que los días 7, 8, 9 y 10 de abril de 1983, se celebrará en el Hotel Condado Holiday Inn el Primer Congreso Puertorriqueño de Cardiología.

A esta actividad científica, auspiciada por todas las Sociedades de Cardiología del país, y por la Escuela de Medicina de la Universidad de Puerto Rico, se darán cita distinguidos invitados de fama internacional y cardiólogos locales para discutir los más recientes adelantos en el diagnóstico y manejo de las enfermedades cardiovasculares de adultos y niños.

Entre los temas a discutirse se han seleccionado los de más relevancia en la práctica diaria, como: Enfermedad Coronaria, Muerte Súbita, Hipertensión Arterial, Marcapasos, Arritmias y Agentes Antiarrítmicos, Farmacoterapia Cardiovascular, Enfermedades Valvulares, Fallo Cardíaco, Enfermedades Congénitas, y otras enfermedades con que comúnmente se confronta el médico en su práctica diaria.

Este evento científico ha sido diseñado de tal manera para que sea de utilidad para Cardiólogos, Internistas, Cirujanos Cardiovasculares, Médicos de Familia y Generalistas.

Gracias a los patrocinadores, esta actividad educativa se ofrecerá a un precio módico para que se beneficie el mayor número de médicos de la comunidad. Los asistentes al curso recibirán 20 horas crédito en Categoría I.

Próximamente recibirán más información sobre esta histórica actividad, esperamos reserven la fecha en su calendario.

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# ASOCIACION MEDICA DE PUERTO RICO

# BOLETIN

## INSTRUCCIONES PARA LOS AUTORES

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuerzen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

### Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquina a doble espacio; por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

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Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

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sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington, DC, May 3-7, 1971. 12. Pollak CP, McGregor PA, Weitzman ED: The effects of flurazepam on daytime sleep after acute sleep-wake cycle reversal. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, June 30-July 4, 1975. 13. Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

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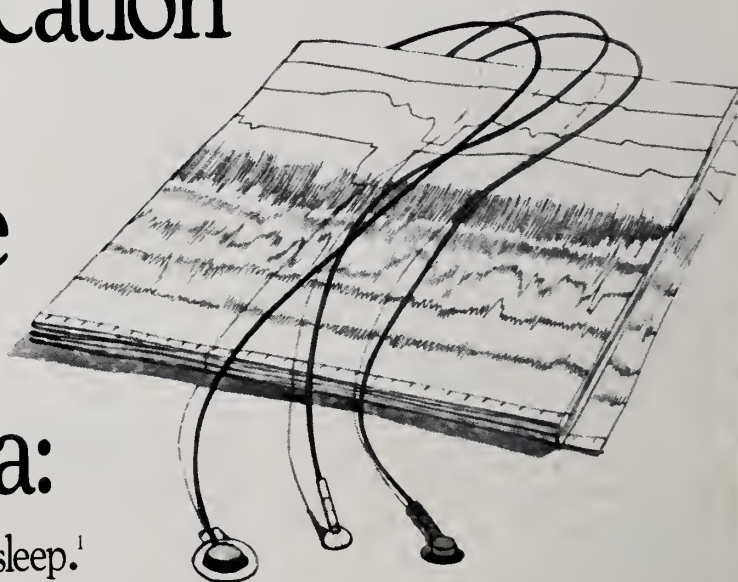
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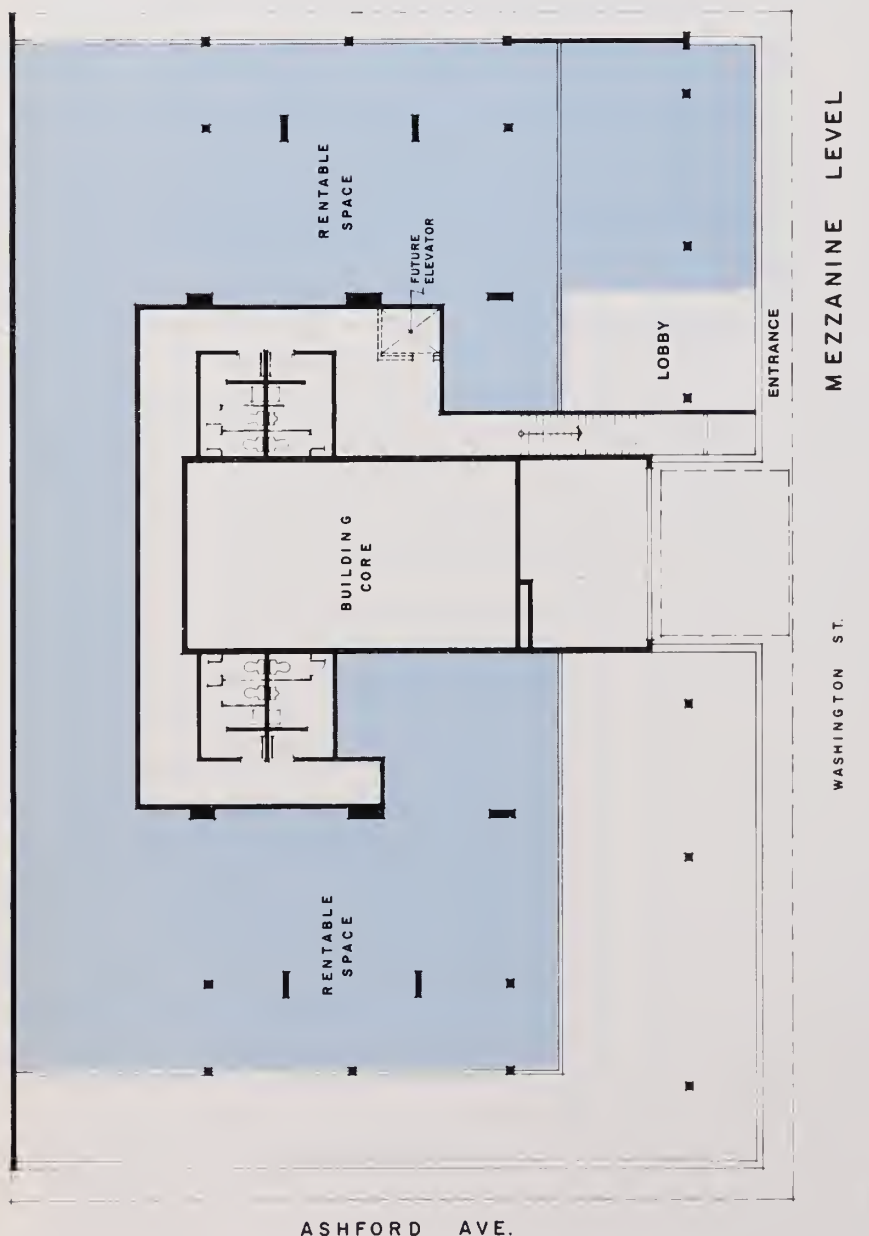
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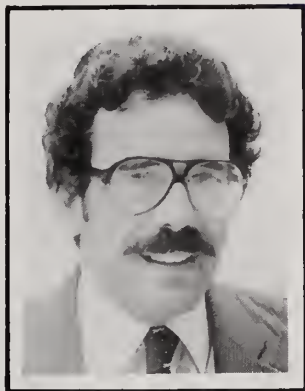
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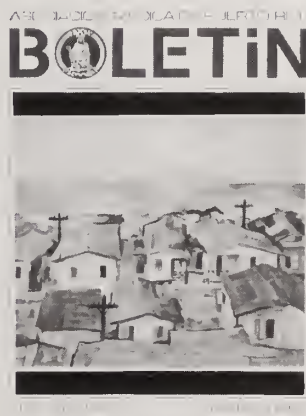
En este número aparecen dos secciones nuevas en nuestro Boletín. Una de ella la hemos llamado "Pathology Review" y estará a cargo de la Dra. María Castillo, Profesora de Patología de la Escuela de Medicina de la Universidad de Puerto Rico. Esta sección tendrá un formato flexible, estará invariablemente bien ilustrada y enfatizará la relación clínica y anatomo-patológica de las enfermedades. Estamos convencidos que las aportaciones de la Dra. Castillo ampliarán la dimensión académica de nuestra revista.

La otra sección nueva es "Nuestro Pasado Médico Histórico" a cargo del Dr. Francisco X. Veray, Cardiólogo, Profesor de la Escuela de Medicina de la Universidad de Puerto Rico y reconocido experto en la vida y la obra del Dr. Ramón Emeterio Betances. Con esta sección el Boletín contribuirá junto con el Dr. Veray a la divulgación de la historia de la medicina puertorriqueña que forma parte de nuestro patrimonio cultural.

Se publican en este número los resúmenes de los temas libres a presentarse en el Primer Congreso Puertorriqueño de Cardiología y algunos de los trabajos presentados en la Conferencia Mundial de la Unión Internacional Contra la Tuberculosis celebrada en Buenos Aires, Argentina en Diciembre pasado.

Estas innovaciones junto con la calidad de los artículos de nuestras secciones fijas son índice del dinamismo y actitud progresista de nuestro órgano oficial.

Rafael Villavicencio, M.D.  
Presidente Junta Editora  
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## NUESTRA PORTADA:

En nuestra portada, el óleo sobre tela titulado "Techos de la Perla" del pintor puertorriqueño Félix Rodríguez Báez (Felo R). El artista es oriundo de Cayey y realizó estudios de dibujo y pintura en la Academia de Arte Edna Coll de San Juan. Co-fundador del Centro de Arte Puertorriqueño en 1950 y mas adelante del Taller Galería Campeche, ambos en el Viejo San Juan donde el artista reside actualmente dedicándose por completo a su trabajo de pintor.

Trabajó por muchos años en los medios de comunicación social, especialmente en la televisión donde se desempeñó como Escenógrafo, Director de Producción, Programación y Operaciones en los canales 4, 7 y 6. Durante los años en que trabajó para los medios de comunicación masiva nunca dejó de pintar y exhibir su obra tanto individual como en colectivas en Puerto Rico y en el extranjero. Esta representado con sus obras en colecciones privadas e institucionales destacándose entre otras; el Museo de Arte de Ponce, el Museo de Bellas Artes de Puerto Rico, la Universidad de Puerto Rico, la Universidad Interamericana, Colecciones de Arte Puertorriqueño del Banco Chase Manhattan, Continental Bank de Illinois y Cooperativa de Seguros Múltiples de Puerto Rico. Fue Director de la Escuela de Artes Plásticas del Instituto de Cultura Puertorriqueña hasta el año 1981. Actualmente ofrece una muestra de carácter retrospectivo en el Instituto de Cultura Puertorriqueña, de uno de los temas más importantes para él, La Perla. De esta misma serie es la obra que reproducimos. Vemos en la misma la imagen quizás mas conocida de esta barriada, los techos que se ven desde lo alto de las murallas del Viejo San Juan en el Boulevard del Valle, mirando al Atlántico, los techos de la Perla. Las obras del pintor Félix Rodríguez Báez son representadas por el Taller Galería André en el Condominio El Centro en Hato Rey. La Asociación Médica de Puerto Rico agradece al Sr. Andrés Marrero, Director de dicha Galería y al artista por su colaboración con nuestra revista.

# EDITORIALES



## Implantación de Colágeno Inyectable

Alrededor de cinco años atrás se introdujo en el mercado estadounidense y particularmente en el estado de California un producto de colágeno inyectable, conocido por el nombre de Zyderm.

Este producto, manufacturado por la Collagen Corporation es obtenido de la piel bovina, altamente purificado, soluble en pepsina y suspendido en solución salina que contiene 0.3% lidocaína. Por su constitución está catalogado como un implante.

A principios del 1982 la Administración de Alimentos y Drogas Federal (FDA) permitió su mercadeo fuera de los Estados Unidos y es así como llega a Puerto Rico.

El fabricante es muy enfático en varios puntos de este material. En primer lugar requiere una prueba cutánea y debe observarse por un período de 4 semanas. El médico debe obtener del paciente un historial cuidadoso de sus antecedentes alérgicos así como enfermedades tales como artritis reumatoidea, lupus eritematoso, tiroiditis de Hashimoto, colitis ulcerativa, enfermedad de Graves, poliarteritis nodosa, síndrome de Reiter, enfermedad de Crohn, síndrome de Sjogren y escleroderma.

Zyderm puede usarse en cicatrices de acné, que no sean del tipo de pincho de hielo ("ice pick scars") cicatrices de varicela, cicatrices post-traumáticas, debajo de injertos de piel en algunas arrugas en la cara resultado del proceso de envejecimiento.

El material viene preparado para usarse en una jeringuilla de tuberculina de 1.0cc. y se inyecta intra-cutáneo y subcutáneo según esté indicado.

Se han reportado reacciones adversas tales como urticaria migratoria. Además se han reportado casos de dolores musculares, fiebre y dolores en las articulaciones que han durado varios meses.

Posiblemente la reacción más adversa ha sido el endurecimiento del implante, produciéndose nódulos subcutáneos que son tan o más objetables que la lesión original.

Es importante señalar que este no es un material para hacer desaparecer cicatrices. Señala el fabricante además que alrededor de los ojos y los labios es donde los resultados son menos favorables. Desafortunadamente, en estas últimas dos regiones es donde la mayor parte de los pacientes desean recibir el implante. Complacer al paciente a sabiendas que el resultado ha de ser mediocre o inefectivo sin duda habrá de desprestigiar un producto de mucha utilidad. En otras palabras, es imperativo que seamos selectivos en la aplicación del implante de colágenos y que esto no se le implante a todo aquel que lo solicita.

*Walter Benavent, M.D.*  
Walter Benavent, M.D.

## "Pathology Review"

En el desempeño diario de la práctica médica, la sintomatología del paciente mezclada con su compleja esfera afectiva y socioeconómica es tan importante, que a veces relegamos los detalles del mecanismo de las enfermedades. Sabemos que cada enfermedad orgánica tiene un substrato de daño celular y que los síntomas, signos y alteraciones en los resultados de laboratorio son las expresiones de una condición patológica.

"Pathology Review" es el título que hemos escogido para una sección nueva del Boletín donde por medio de ensayos, discusiones, demostraciones, fotografías, etc., pondremos de relieve la importancia clínica de la patología. Daremos énfasis no solamente a los cuadros morfológicos, macroscópicos y microscópicos, sino también a las pruebas de laboratorio necesarias para llegar a un diagnóstico. Esperamos con esta sección ofrecer información que permita a nuestros lectores mantenerse actualizados con la patogenia de condiciones clínicas más o menos comunes y les ayude al hacer un diagnóstico diferencial cuando se enfrenten con entidades clínicas que presentan cuadros similares.

La aplicación de la tecnología moderna a la medicina de laboratorio es actualmente rápida, sofisticada y cambiante lo cual hace a veces difícil, que entendamos, todos aquellos servicios útiles que el laboratorio puede ofrecer.

Será también uno de nuestros objetivos discutir diferentes metodologías diagnósticas de laboratorio y el papel del patólogo en su interpretación.

Aunque trataremos de escribir nuestra columna en español, siendo nuestro Boletín una revista bilingüe habrá ocasiones en que usaremos el idioma inglés.

Para poder cumplir a cabalidad con los objetivos que intentamos desarrollar en esta sección, nos gustaría conocer las preferencias de nuestros lectores en cuanto a las condiciones clínicas o enfermedades que les agradaría se discutieran. A tales propósitos, agradecemos toda comunicación escrita sobre este particular que nos ayude a ofrecerles una sección de patología que responda a las necesidades de ustedes.

Sobre la marcha se introducirán aquellas innovaciones que permitan hacer del "Pathology Review" una instrumento de ayuda al clínico cuando evalúa, diagnostica y maneja un enfermo.

Aprovecho estas líneas para agradecer a la Junta Editora del Boletín, y especialmente al Dr. Rafael Villavicencio, el haberme brindado la oportunidad de compartir con ustedes nuestra columna científica "Pathology Review".

*María Castillo, M.D.*  
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# ESTUDIOS CLINICOS

## Clínico-Epidemiological Features of 102 Consecutive Cases of Ulcerative Colitis in Puerto Rico

Carlos Micames M.D.  
Juan Zaiter M.D.  
Adan Nigaglioni, M.D.

**Summary:** The experience at the Puerto Rico Medical Center in 102 cases with definite diagnosis of ulcerative colitis recorded from 1974 through 1980, were reviewed. There were 59 women and 43 men having a mean of 7.8 years with the disease.

Rectal bleeding, diarrhea and abdominal pain were major initial complaints. The intermittent clinical course was the most frequently found. Eighty-four patients required hospitalization, and twenty-two of them had surgery, five on an emergency basis.

The most frequent systemic complications were anemia, arthralgia and chronic liver disease. The local complications were: eight colonic strictures, seven perianal diseases, three toxic megacolons, and two inoperable carcinomas. Five patients died from causes related to colitis.

This study suggests that ulcerative colitis is not uncommon in Puerto Rico, that the sigmoidoscopic appearance could be confused with endemic entities such as schistosomiasis and tropical sprue, that the outlook of the disease in the tropic is similar to other geoeographical areas, and aggressive carcinoma continues being a prevalent undesirable complications considering the prevalence of this neoplasia in the island.

Differences have been found in the clinico-epidemiological aspects of Ulcerative Colitis in previously defined communities; for example, United States white Army officers are affected approximately twice as frequently as white men, but there is no difference in prevalence between white and black enlisted men<sup>1</sup>. In the city of Baltimore ulcerative colitis is less fre-

quent in the black than in the white population and more frequent among jews.<sup>2</sup> In New Zealand ulcerative colitis is more prevalent among the population of European extraction than among the Maoris.<sup>3</sup> Reports in the literature from other parts of the world.<sup>4-11</sup> have attempted to establish that hereditary or environmental factors influence the clinical course or prognosis of the disease. In order to get some information about the clinical and epidemiological features of ulcerative colitis in Puerto Rico, we considered pertinent to review a relatively large number of cases from the two major general hospitals of the Puerto Rico Medical Center. Because of the wide base of referral of these institutions, it is likely that the clinical information reflects the behavior of this disease in the whole island.

### Material and Methods

The medical records of 116 patients with the sigmoidoscopic diagnosis of ulcerative colitis were reviewed. These patients had been evaluated at the Gastroenterology Sections of University District Hospital and San Juan City Hospital, between June 1974 and February 1980.

Information was abstracted and coded under the following subjects: age, sex, site of residence, occupation, age at onset or the disease, and at the time of diagnosis, initial symptoms, number and length of hospitalizations, complications, extension of intestinal lesions, associated diseases and surgical treatment if any.

The disease was staged according to the extent of colonic involvement: Type I: proctitis; Type II: proctosigmoiditis; Type III: left sided colitis (from middle transverse colon downward); and Type IV: universal colitis. The extension was determined by colonoscopy, barium enema was used for staging only when the whole colon appeared involved.

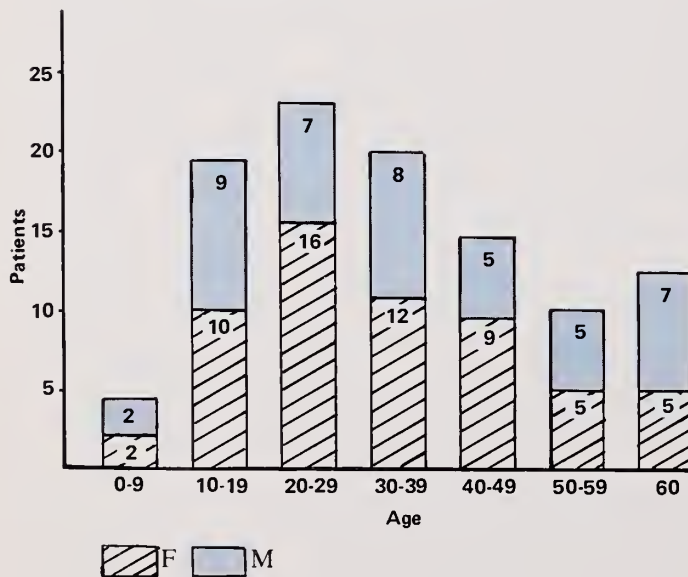
### Results

From the original 116 cases of suspected ulcerative colitis, only 102 patients fulfilled the criteria of definite ulcerative colitis as defined by Mendeloff et al.<sup>12</sup> There were 59 women and 43 males having a mean of 7.8 years with the disease. Fourteen cases were excluded for the following reasons: insufficient evidence to justify the diagnosis (8), shistosoma proctitis (2), granulomatous colitis (1), salmonella enteritis (1), sigmoid colon diverticulitis (1), and tropical sprue (1).

### Age, sex, and occupation of the patients

Sixty-two patients developed the disease between the ages 10 and 39 years. Most patients were in the third decade at the time of the onset of symptoms (Figure 1). Females were affected more frequently than males with a ratio 1.3:1. Race was clearly designated in only 82 of the 102 analyzed cases (Table 1). Only 37% of the white patients and 42% of mulattoes developed the disease younger than 30 years old, while 68% of the black patients developed the disease before age 30. Mean age of onset among whites was 37.3 years and blacks 26.6 years. The majority of males were office workers and students, followed by mechanical operators; among females, housewife was by far the most frequent occupation, followed by office worker and students.

**FIGURE 1**  
Incidence by Age and Sex



**TABLE 1**

Race Distribution in our Group of Patients			
Race	Females	Males	Both
Albinos	1	2	3
Blacks	9	7	16
Whites	28	20	48
Mulattoes	10	5	15

### Site of residence

All the patients were residents of Puerto Rico, 53 came from the metropolitan area of San Juan and 49 from the eastern, central and northern regions of the island.

### Initial Symptoms and Extension of Intestinal Lesions

The most common complaint at the onset of ulcerative colitis was rectal bleeding. It was present in 95 patients, followed closely by diarrhea and abdominal pain (Table 2). If symptoms are analyzed in relation to the extent of colonic involvement, fever was observed as part of the initial picture more frequently in patients with universal colitis, while tenesmus was a more prominent symptom in cases of proctitis and proctosigmoiditis.

**TABLE 2**

Initial Symptoms	
Symptoms	No. of Patients
Rectal Bleeding	95
Diarrhea	93
Abdominal Pain	75
Weight Loss	63
Tenesmus	58
Fever	25
Vomiting	18
Fecal Incontinence	8

### Hospitalization and Operation

Eighty four of the 102 patients required hospitalization at some point during the six year study period. The frequency of hospitalizations in this sub-group ranged from one to nine with an average of 2.3. The average length of hospitalization for the 84 patients during the study period was 43.3 days. Eighteen patients were never hospitalized. Only 4 of these patients had extensive colitis (Types III and IV), the others had proctitis and proctosigmoiditis.

Colonic resection was performed on 22 patients, two of whom required three operations. Total proctocolectomy with ileostomy was performed in 18 patients. Three patients died postoperatively. Emergency surgery was required in 5 cases because of massive bleeding peritonitis with colonic perforation, or toxic megacolon. The most common indication for operation was intractable disease, followed by inflammatory rectal strictures (Table 3).

**TABLE 3**

Patients Needing Surgical Treatment	
<u>Elective:</u> 17 patients	
Intractable Bleeding	
Strictures	
<u>Emergency:</u> 5 cases	
Massive Bleeding	
Megacolon	
Colonic Perforation	



### Clinical Course, Complications and Associated Diseases

The duration of symptoms before the diagnosis of ulcerative colitis was first recognized is shown in the Table 4. The diagnosis was usually established within the first six months of symptoms but, in the oldest of our patients, it took four years history of intermittent bloody diarrhea before the diagnosis was suspected. The clinical course was classified according to Michener et al,<sup>13</sup> and is shown in Table 5. The most common clinical course was the intermittent type.

TABLE 4

#### Duration of Symptoms Before Diagnosing Ulcerative Colitis

Duration	Females	Males
< 12 months	45	31
> 12 months	14	12

Twenty-one patients had local intestinal complications. Eight had strictures, six of them located in the rectal area and the other two in the transverse colon. Two had inoperable carcinomas. Seven patients had perianal disease and three developed toxic megacolon. Anemia was by far the most frequent systemic complication (Table 6).

Five of the 102 patients died during the six year study period as a direct consequence of the colitis. Three died postoperatively being the indication for surgery fulminant colitis in two and toxic megacolon in one case. The two patients that developed carcinoma of the colon in the course of the ulcerative colitis succumbed to this tragic complication.

TABLE 5

#### Clinical Course (Michener Classification)

Clinical course	Females	Males
Single Episode	5	10
Intermittent	26	16
Chronic not Incapacitating	13	11
Chronic Incapacitating	15	7

TABLE 6

#### Complications

Systemic	Patients
Anemia	69
Arthritis or Arthragia	13
CALD	6
Nephrolithiasis	5
Thrombophlebitis	3
Pyoderma gangrenosum	3
Erythema nodosum	3
Epyscleritis	1
Local	
Colonic Strictures	8
Perianal Disease	7
Toxic Megacolon	3
Carcinoma	2
Colonic Perforation	1

#### Discussion

This study tends to suggest that the natural history of ulcerative colitis in a tropical area does not differ significantly from that seen in temperate zones of the world.<sup>14</sup> In our clinical material there is a female preponderance in accordance with the more representative studies<sup>2, 4, 6</sup> and in this respect a variance with the regional studies from Minnesota<sup>7</sup>, Norway<sup>8</sup> and Turkey.<sup>10</sup> The exclusion of fourteen patients from the study group was necessary to eliminate those cases in whom the diagnosis of ulcerative colitis was in doubt. In our geographic location where other endemic condition frequently affect the large intestine, it is very important to exclude those entities which may at some point during clinical course, mimic ulcerative colitis. Careful follow up with repeated sigmoidoscopies is the best way to truly identify those cases in whom the diagnosis of ulcerative colitis is not based on strong criteria.

Although the clinical records reviewed contained a classification of patients into racial groups; in an environment like ours where there is such a marked racial heterogeneity, the value of this information is limited. The observation that of those patients classified as black, 68% began with the disease before the age of 30, may represent an important point to study further. This is so because generally the younger the patient the more likelihood of having extensive disease<sup>16</sup> and because of increased cumulative risk of cancer in ulcerative colitis beginning at an early age.<sup>18-21</sup> We did not compare barium enema and endoscopy in terms of establishing extension of colonic involvement, but there was a good correlation of colonoscopic and radiologic findings with extensive disease.

Correlation is poor with less intestinal involvement specially proctitis and proctosigmoiditis when sometimes barium enema is reported as normal. The routine use of colonoscopy to establish extent of disease is probably not necessary in the majority of cases. In terms of symptomatology, clinical course, complications, and need for surgery our group is comparable with those reported in the literature. It is noted however that only two cancers were found in the whole group. This low figure could probably be explained on the variable lenght of disease of our patient population.

In summary, this study shows that ulcerative colitis is not a rare entity in Puerto Rico; that it needs to be differentiated from other common endemic conditions affecting the large intestine; and that it's clinical features are not very different from those seen in other parts of the world.

**Resumen:** Se revisaron los expedientes clínicos de 102 pacientes con diagnóstico de colitis ulcerativa, 59 pacientes eran de sexo femenino y 43 de sexo masculino, con un promedio de 7.8 años de enfermedad.

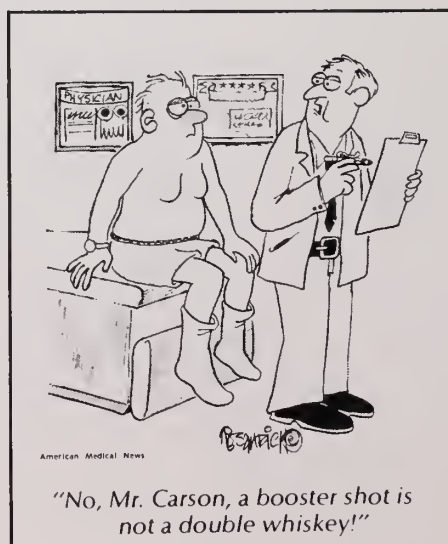
El sangramiento rectal, diarrea y dolor abdominal fueron los síntomas iniciales más comunes. El curso clínico intermitente fue el mas frecuente. 22 pacientes requirieron cirugía, 5 en calidad de urgencia.

Las complicaciones sistémicas más frecuentes fueron anemia, artralgias y enfermedades hepáticas crónicas; mientras que las locales fueron: estrecheces crónicas, enfermedad perianal, megacolon tóxico y 2 carcinomas inoperables, 5 pacientes murieron por causa de su colitis.

El estudio muestra que la colitis ulcerativa no es rara en Puerto Rico, que su apariencia sigmoidoscópica puede confundirse con otras entidades endémicas, que el comportamiento de la colitis en el trópico es similar al de otras áreas geográficas y que el carcinoma invasivo continua siendo una complicación indeseable, considerando la prevalencia de esta neoplasia en la isla.

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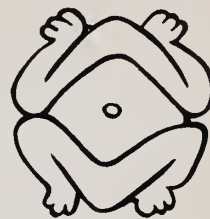


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# Nuestro Pasado Médico Histórico



## Betances, El Médico

Francisco X. Veray, M.D.

*Trabajar es producir y producir es servir a la humanidad. Producir cuanto uno pueda y hacer el bien que uno pueda es llenar la vida de un ciudadano y de un hombre de bien. —Don Ramón Emeterio Betances.*

Don Ramón Emeterio Betances fue uno de esos hombres de los que se puede decir<sup>1</sup> “que son superiores a su pueblo y a su tiempo”. La figura de este noble atleta del trabajo intelectual y revolucionario ha sido estudiada en las diferentes facetas de su personalidad, pero nadie lo ha considerado, en la que para mí resulta la más interesante que es la figura de Betances como médico. Resulta curioso constatar, que las diversas descripciones que hemos leído de su carácter tales como: “un hombre de figura venerable, de mirar dulce escudriñador, de hablar pausado con capacidad de escuchar y de no emitir juicio alguno hasta no haber oído hasta la saciedad su interlocutor”,<sup>2</sup> corresponden en parte a las cualidades que se supone requiera un buen médico, ya que es difícil desligar a un hombre de ciertos y determinados rasgos, de una forma de actuar que se adquiere en la brega diaria de una disciplina.

A pesar de que la figura médica de nuestro gran revolucionario yace olvidada para la mayoría de los puertorriqueños, creo resulta interesante dar a conocer el renombre que alcanzó como eminente médico que fue de su época.

A partir del 1848, se trasladó a París y empieza a estudiar su carrera en la Facultad de Medicina. Tuvo como profesores a los siguientes médicos: Dr. Arístide Verneuil, (1923-1895) Ayudante a Cátedra de Anatomía y Profesor de Patología a quien le debemos *Recherches sur la Locomotion de Coeur* (1852) y cuyo libro *Memoria de Chirurgie* fue texto de cirugía para entonces;<sup>3</sup> Dr. Paul Broca (1824-1880), Profesor de Patología Quirúrgica, a quien se le debe parte de los estudios más significativos de la anatomía del cerebro;<sup>4</sup> Dr. Charles Pijot (1816-1876), Profesor de Obstetricia y Ginecología (1845),<sup>5</sup> Dr. Louis Jules Behier (1813-1876), Profesor de Medicina Interna, quien en 1874 practicó las primeras transfusiones en Francia con éxito.<sup>6</sup>

Si nos detenemos en este recuento de los profesores de Betances, es para recalcar con el Profesor Laín Entralgo, como en la primera mitad del siglo XIX Francia vio una constante sucesión de brillantes médicos y de notables cirujanos. “París era la cuna de la medicina de la época y tan

pronto ascendía un cometa, centellaba otro más brillante y poderoso robando lustre a aquel primero”.<sup>7</sup> El Dios de la Medicina que una vez se había asentado en Grecia y Alejandría, ahora lo hacía en París. España languidecía en garras de un absolutismo que cerraba universidades, acababa con academias y arremetía contra los escasos destellos de la Ilustración, haciendo fusión entre los médicos de universidad y sangradores. Este era el panorama de la medicina mundial en los tiempos que Betances se formaba.

El profesor Weeker de Oftalmología una vez viendo trabajar a Betances, dijo: “No hay entre los americanos del Sur nadie que tenga esa habilidad la cual parece que le es innata”.<sup>8</sup>

Fue compañero de promoción del doctor Paul Joseph Lorain (1829-1875) quien en 1866 usa por primera vez los líquidos intravenosos para reponer la pérdida de éstos en el tratamiento del cólera y en 1872 sucede a Daremberg en la cátedra de Historia de la Medicina en la Facultad de Medicina de París; de León Labbe, cirujano célebre francés, uno de los primeros en practicar la gastrotomía en Francia, quien fue íntimo del doctor Betances hasta el fin de sus días y quien lo presentó a la Academia de Cirugía y al célebre Jean Martin Charcot (1825-1893) a quien le debemos los estudios más renombrados de anatomía patológica del sistema nervioso.<sup>9</sup>

Estudia Betances en medio de una juventud liberal, siendo testigo de la Revolución de 1848, que le obligó a hacer una pausa “para reflexionar sobre el servilismo en el cual se encontraba su pueblo y las iniquidades sometidos por un poder personal sin vergüenza, haciendo que su alma generosa se revelara” según Bonafoux, artículo del *l’Echo Poliglote*, 20 de diciembre de 1891.<sup>10</sup>

En 1853 se doctoró en Medicina y Cirugía en la Facultad de París y presenta su tesis sobre “Las causas del aborto”.<sup>11</sup>

El 9 de abril de 1856 está de vuelta en Puerto Rico obteniendo la convalidación de su título ante la subdelegación de Medicina y se establece en Mayagüez.<sup>12</sup>

Betances introdujo en Puerto Rico las ideas de las escuelas francesas de mediados del siglo XIX, trajo la semilla de la Medicina Anatomopatológica tan en boga en ese tiempo.

La medicina puertorriqueña de principios del siglo XIX era una medicina atrasada y sumida en el mayor oscurantismo. Diversos factores, como había indicado, contribuyeron a ello, y vemos que la llegada del absoluto Fernando VII al trono español constituyó un “período de desastre”, (López Piñero y García Ballester, *Medicina y Sociedad en la España del siglo XIX*) para la medicina española.<sup>13</sup>

El absolutismo pone fin a los adelantos que trajo la Ilustración y trajo la desorganización y destrucción de las instituciones científicas. El gobierno absoluto al tratar de poner coto al liberalismo de los médicos y figuras de renombre, consigue que éstos vean sus esfuerzos ahogados de hacer

algo de verdadero valor científico. Esta medida trajo una gran escasez de médicos y se intentó solucionarlo creando "El Cuerpo de Cirujanos Sangradores" para pequeñas localidades y la "Reunión de Facultades", fusión de los físicos y los cirujanos.<sup>14</sup> Si esto sucedía en la Madre Patria es fácil imaginarse el panorama de la medicina ejercida en Puerto Rico, en donde había que añadir a la distancia de la metrópoli, la falta de facultades médicas organizadoras y regidoras y una serie de gobernantes que con sus absurdas leyes prohibían la entrada de libros e información en la Isla, tratando quizás de seguir así el letargo intelectual en que estaba sumido el pueblo. La medicina en Puerto Rico generalmente se ejercía en forma irregular y a veces torpe por prácticos, curiosos y charlatanes. Existían médicos de título universitario y esos pocos estaban concentrados en su mayor parte en la capital, y casi todos pertenecían a la sanidad militar, fieles servidores al régimen.

En 1804 la Medicina tuvo un momento de esplendor al conseguir el Dr. Francisco Oller, con la ayuda del Brigadier don Ramón de Castro, imponerse a las exigencias de don Francisco Javier de Bálmis y Berenger por haber empezado a vacunar contra la viruela en Puerto Rico antes que "La Expedición Filantrópica a América", constituida con el mismo fin, llegase el 9 de febrero de 1804.<sup>15 16</sup>

El otro hecho importante de esta década es la institución de una cátedra de Medicina por los doctores José Ma. Espaillet y José Ma. Vargas, que cierra en 1845 para dar paso a una escuela de cirujanos o de médicos prácticos que en aquel momento hacía más falta.

En 1839 por Real Decreto se crea la Subdelegación de Medicina; el Gobierno de Madrid trataba sí de ponerle fin a las prácticas fraudulentas de charlatanes y curanderos. Al pasar el tiempo, la labor de este cuerpo se convirtió en un sistema de vigilancia tipo policía médica, más que en el organismo rector y promotor de aptitudes. Ejemplo de esto nos lo da Quevedo Sáez con la prohibición, sin sentido, por este organismo, de la obra de Cayetano Cruixent, "Reflexiones sobre los Sistemas y sobre el Ejército de dicha Ciencia". Los miembros de la Subdelegación ya que en esta memoria se tocaban personalidades médicas de la capital, alegaron que las esculturas de don Antonio Venegas eran indecorosas y "una afrenta al buen vivir ciudadano".<sup>17</sup>

No fue hasta 1895 que se publicó la primera Revista Médica llamada Revista Médica editada por Don Francisco del Valle Atilés.<sup>18</sup>

La medicina española, que a principios del siglo pasó por un período catastrófico, empieza en la segunda mitad a tomar un auge inmenso, terminando el siglo con el período conocido como "La Generación de Sabios".<sup>19</sup>

El horizonte médico puertorriqueño no tomó esos derroteros. Betances traía las ideas de Bichat: "La vida es el conjunto de propiedades vitales que resisten a las propiedades físicas".<sup>20</sup>

La enfermedad no era más que una alteración de las propiedades vitales. Si estos fenómenos físicos triunfaban sobreviene la muerte y el equilibrio de éstas era la salud". La curación se obtenía cuando estas propiedades recobran su hegemonía.

Recordaba las enseñanzas de Brouissais, Cruveilhier, Chauffard y Laennec, todos iniciadores de la clínica moderna basada en la fisiología y la patología.<sup>20</sup>

Traía Betances muchos recursos para diagnosticar, pero se quedaba como todos los de su época, corto en materia de terapia en el arte de curar.

En 1855 surge una epidemia de cólera en Puerto Rico, que según el Dr. Henri Dumont, comenzó en Naguabo, pueblo de la zona oriental de la isla, foco del negocio de reses. Dumont dice "vino de St. Thomas o de Venezuela, que tomó la ruta de la dirección de los vientos y el curso de los ríos", causando más estragos en donde lo denso de la población era mayor según la condición baja o pantanosa del terreno. El curso de la epidemia fue el siguiente, según los pueblos: Naguabo, Bayamón, Arecibo, Aguadilla, Naguabo otra vez, Humacao, San Juan, Manatí, Vega Baja, Arecibo, Aguadilla, otra vez Naguabo, Arroyo, Ponce Mayagüez y Utuado. Causó verdaderos estragos en Caguas. Cosa rara siendo ésta una ciudad del interior.<sup>21</sup>

Cruz Monclova nombra a Betances entre los médicos que se distinguieron en la epidemia.<sup>22</sup>

A Mayagüez llegó el cólera hacia 1859 y cuenta el Dr. Block, médico de Sanidad de Puerto Rico "que en aquella ciudad se presentó de manera fulminante". Las características clínicas con que se presentaba era en una forma mucosa diarrea y en su forma tóxica con intensos calambres.<sup>23</sup>

En esta epidemia resaltó Betances sus dotes de clínico y médico competente. Dice María de Angelis "La ciudad de Mayagüez lo vió como un ángel caer en el fondo de la epidemia, luchar bravamente sin temor al contagio".<sup>24</sup>

En las horas diurnas fatigaba cinco caballos para acudir a todas partes donde se le llamaba. (Cosa que el mismo Betances sustenta en una de las cartas que recopila Carlos M. Rama en "Las Antillas para los Antillanos").<sup>25</sup>

No se limitó su obra exclusivamente al tratamiento prescrito para esa enfermedad, sino, la estudió e hizo interesantes observaciones. En 1884 publicó un interesante trabajo en París sobre el cólera titulado "El cólera", como fruto de esta experiencia".<sup>26</sup>

En el tratamiento de cólera abogó por los eméticos como la ipecacuana. Recomendaba que "los esfuerzos del médico se debían dirigir a detener el vómito y la diarrea" y recomendó la medicación opiada antidiarreica. Usaba el láudano, el polvo de opio y el elixir paregórico, para estos menesteres. Recomendaba el hielo, la champaña helada para contener el vómito y contra las diarreas, llegó a usar lavativas de vino caliente de Burdeos. Siguiendo los estudios del Dr. P. Vigier, creyó en empleo de la llamada "limonada sulfo carbonatada" como medicación antimicrobiana.<sup>27</sup>

Abogaba por la asistencia asidua fundada en la observación repetida y rigurosa, amén de la vigilancia incansable que permite escoger el momento propio para "la más eficaz aplicación del remedio".<sup>28</sup>

En 1858, con la ayuda de su adversario político don Antonio Blanes, fundó en Mayagüez La Casa de San Antonio que estaba situada entre las Calles de Mirasol y De la Rosa y a la que más tarde se le agregó una escuela de párvulos. Este hospital tenía cabida para 40 camas y se sostenía por legados y obras de beneficencia, según nos cuenta Cruz Monclova.<sup>29</sup>

En 1859 tiene que abandonar la Isla desterrado por su noble ideal y en París en carta a Don C. Cintrón del 15 de septiembre de 1860, le cuenta cómo trabaja como médico y la consideración que le tienen.<sup>30</sup>

Es para esta fecha que muere de fiebre tifoidea su sobrina que iba a ser su esposa. En estos tristes momentos lo acompañan don Francisco Basora, don Antonio Ruiz, Dr. Carbonell, Don Francisco Oller, Sr. Porrata y Sr. Prevost, hijo. Son momentos difíciles para Betances, pero a fines del 1860 puede



regresar a Puerto Rico.<sup>31</sup> Cuenta C. de Lemaire en El Benefactor de Eduardo Neumann Gandía, que se dedicó al estudio de las enfermedades endémicas de los países tropicales, logrando modificar los tratamientos seguidos hasta entonces, para la dispepsia, la disentería, la fiebre tifoidea y el tétano.<sup>32</sup>

Hizo diversos estudios sobre los métodos a seguir en el tratamiento de las enfermedades, adaptándolos a nuestro medio ambiente en los pueblos donde predominaba la fiebre palúdica. Su tratamiento para las neumonías le valió los parabienes del profesor Pecholier de la Universidad de Montpellier.

El 23 de septiembre de 1864 en una asamblea celebrada en la Academia de Cirugía de París según publicó El Progreso de Madrid, el eminente cirujano parisino Dr. León Labbe, discípulo y amigo de Betances, presentó una memoria de Betances titulada "De l'oscheotomie". Este trabajo contiene las observaciones personales del Dr. Betances sobre el tratamiento de la elefantiasis de escroto y tiene tres observaciones principales de osqueotomía, escritas con pormenores y hechas con felicidad. Estas operaciones fueron practicadas en los siguientes pacientes: Fermín Arrocho de 45 años, que fue operado en julio de 1860, don Alejandro Maldonado de Ponce, en noviembre de 1863 y el tercer paciente el mulato José Saturnino Toro de 25 años, también de Ponce que fue intervenido en 1864.<sup>34 35</sup>

Esta monografía fue discutida por una Comisión Especial compuesta por los siguientes doctores: Palaillón, Maro Sie, y León Labbe y fue objeto de calurosos elogios por parte del profesorado. Se elogió la competencia del autor y la nueva luz que arroja acerca del conocimiento y curación de tan terrible mal.<sup>36</sup>

Los pacientes de Betances años más tarde, fueron seguidos en tratamiento y examinados a insistencia del Dr. J. Audinot por el Dr. Henri Dumont, quien en su libro Ensayo de una Historia Médico Quirúrgica de la Isla de Puerto Rico (1875) Capítulo VII, comenta el procedimiento y la terapia empleada con tanto acierto, por el Dr. Betances. Dumont añadió otro caso de un europeo que fue operado por el Dr. Betances en 1862 y a quien suministró la anestesia el médico venezolano Dr. P. Arroyo y que hizo historia por ser la primera vez que en Puerto Rico se usaba cloroformo como anestesia. Dumont pone a Betances a la altura de Larrey, Delpech, Morin y Clot Bey, cirujanos que mundialmente estaban reconocidos como los principales en la materia.<sup>37</sup>

A partir de 1869, comienza un peregrinaje político nuestro ilustre galeno entre Nueva York, Santo Domingo, Curazao, Saint Thomas y a partir de 1872 se estableció de nuevo en París, en un piso de La Rue de Chateaudum. Ahí logra otra vez tener una buena clientela y posición respetable entre los médicos más destacados de la capital francesa. Entre sus pacientes estaba don Manuel Ruiz Zorrilla (1833-1895).<sup>38</sup>

De Bonafoux recogemos la siguiente ficha médica... "el señor Ruiz Zorrilla de 46 años envejecido, 'gordo, se queja de malestar en la región del corazón'. 'No tiene otro síntoma de enfermedad'. 'Ligera dispepsia'. 'Lo ausculto'. 'Al levantar la cabeza se pone pálido'. Se da de hombre apasionado sujeto a fuertes impresiones'. 'Por lo demás nada en el corazón'. Le he ordenado pildoras de quinina y agua de Vichy.<sup>39</sup>

De otra nota de la salud de Ruiz Zorrilla, recogemos: "Esta contento pues está convencido que su enfermedad es mala digestión". El 22 de febrero de 1887 comenta de su visita al paciente; que tiene tos con esputos sanguinolentos. Tiene una arritmia muy fácil de notar al auscultarlo. Después de 3. 4. 10, 20 pulsaciones regulares, hay una detención momentánea. El mismo lo ha notado más de una vez. El 30 de enero de 1890,

Betances da su diagnóstico —sífilis cardíaca—, apunta que el paciente está mejor desde que sigue su tratamiento.<sup>40</sup>

En carta de 1895 al Dr. José María Esquerdo y Zaragoza le da una serie de consejos para el seguimiento de su paciente repatriado; le recomienda "Inyecciones hipodérmicas de líquido orgánico" y le habla de la importancia del digital y de los exámenes de orina.<sup>41</sup>

Es a través de estas concienzudas observaciones médicas, que nos es fácil apreciar sus dotes de clínico y observador sagaz, ya que con el escaso armamentario médico de la época fue capaz de diagnosticar lues cardíaca y una arritmia que hoy creemos fuera debida seguramente al digital que tomaba el señor Ruiz Zorrilla.

Otro eminente paciente del Dr. Betances fue don Eusebio Blasco (1844-1903) periodista y literato español, también emigrado a París y su hija Sofía, a quien salvara la vida una vez. Esta amistad se enfrió por las ideas de Betances, pero nos dice la nobleza de su carácter que en una ocasión cuando Blasco tuvo un accidente, Betances se presentó a atenderlo, retirándose una vez éste estuvo sano.<sup>42</sup>

Por Blasco conocemos el aspecto físico de Betances "Hombre de hermoso aspecto, alto, vestido de negro con una corbata negra, cabeza artística como pocas, cabellos blancos en abundancia y rizados, barba grande y blanca a una edad en que los que no han trabajado ni sufrido la tienen todavía negra", parecía un apóstol. La fisonomía dulcísima; de ojos de tierno mirar". Hablaba en voz baja. Todo en él era evangélico".<sup>43</sup>

Sus inquietudes intelectuales eran grandes y lo vemos haciendo estudios con Dejardin sobre la Euphorbia Mystifolia y la Vicorea Batífera y con la ayuda del sabio naturalista Geoffrey Saint Hilaire estudia la coca y el ramie, estudios que le merecieron felicitación de la Société D'Acclimatation.<sup>44</sup>

También hizo estudios sobre el tétano con Verneuil, que dieron lugar a que el Dr. Manuel Pasarell Rius, médico ponceño, le dedicara a Betances su monografía sobre el tétano.<sup>45</sup>

Con el Coronel Atola y el Ing. Cancio creó un instrumento para airear el agua hervida y de uso durante las epidemias, este invento lo dió a conocer en una sección de la Academia de Medicina de París.<sup>46</sup>

En 1890 publica varios artículos sobre el cólera como lo había ya hecho en 1884. En un Apéndice discute un tratamiento nuevo que no es otra cosa que líquidos intravenosos.<sup>47</sup> En 1886 publicó otra monografía titulada La Uretrotomía, obra donde hace el recuento de sus observaciones sobre pacientes que padecían estrecheces de la uretra debido a males venéreos.<sup>48</sup>

El 1 de julio de 1887 recibe del gobierno francés la Orden Nacional de la Legión de Honor, según carta del Ministro de Asuntos Exteriores.<sup>49</sup>

En 1890 la Revista República publicó una reseña del banquete celebrado el 29 de abril, en honor de las personalidades médicas parisinas del momento, donde Betances hizo el brindis: Terminó diciendo que "como la ciencia es una de las fórmulas del progreso, allí no había ninguno que no fuera combatiente en pro de la perfección humana".<sup>50</sup>

Asistió muchas veces a ministros del gobierno como pacientes exigiéndole como precio de sus servicios el rescate de algún patriota antillano preso. Fueron sus pacientes: Gambetta, Favre, Humbert y Berthelot.<sup>51</sup>

La Revista francesa L'Echo Polyglote cita en el 20 de diciembre de 1891, dos obras científicas de Betances, una titulada la Vacuna y la otra El Tratamiento de la Tuberculosis, pero no tenemos constancia de la existencia de ninguna de

ellas; también comenta este mismo periódico las gestiones llevadas a cabo por Betances para crear en París un hospital latinoamericano.<sup>52</sup>

Hasta Madrid llega la fama de nuestro médico como lo demuestra el periódico El País, que en 1891 publicó que "Betances es una de las más importantes y conocidas personalidades que figuran al frente de la ciencia europea".<sup>53</sup>

Existen dos anécdotas que demuestran cómo su adiestramiento médico se refleja en todos los aspectos de su vida. Dice en sus observaciones: "la calumnia es como el sarampión que desde que brota deja de ser peligrosa". Cuando alguien le preguntó: "Maestro, usted que ha pasado a través de tantas emboscadas, traiciones e infecciones, ¿es que tenía usted un preservativo? ¿Dígame, cuál? Y Betances le contestó: "La limpieza tanto en lo físico como en lo moral".<sup>54</sup>

Estaba tan entregado a su ideal que fue aportando todo su capital por la causa que desde París luchaba. Al morir carecía de todo a pesar de haber tenido gran éxito por sus aciertos médicos.

A esa vida que llevaba tan llena de trabajo, de preocupaciones, se unieron los últimos acontecimientos políticos de esta Isla, que tanto quiso y "la disnea fue venciendo" y "matándole el corazón".

No sabemos a ciencia cierta cuál pudo ser la causa de su muerte, pero basándonos en su carta a don Julio Henna del 24 de mayo de 1895, dice que tenía uremia. Atando cabos de los síntomas descritos por Bonafoux, quien describe disnea, palidez blanquecina a más de su edad y que venía enfermo desde 1892, como escribió en su carta a don Eugenio María de Hostos cuando tuvo un acceso de gota, "más fuerte que nunca" y "que lo había dejado anémico, debilitado, andando con pena y lleno de vejez". Todo esto nos hace pensar en fallo renal con insuficiencia cardíaca congestiva.<sup>55 56</sup>

Cuando cayó enfermo de gravedad lo llevaron a una casa de salud en Neuilly, pero lo trasladaron a su piso de París días más tarde, donde murió el 18 de septiembre de 1898, viernes, a las 10:00 de la noche.<sup>57</sup>

La medicina que ejercía el Dr. Betances como podemos ver a través de su obra y de su epistolario preservado por Bonafoux, Guzmán Rodríguez y Carlos Rama, era una medicina altamente científica basada en los fundamentos de los más conocidos y depurados investigadores del momento, teniendo como pilares la observación clínica y el estudio anatomopatológico. Medicina y comportamiento clínico que nos lleva a pensar que Betances, junto a José María Vargas, venezolano de heroica estirpe, y Henri Dumont, francés afincado en Puerto Rico, son los fundadores de la medicina académica puertorriqueña. Su ejemplo sigue vivo en los que como él creemos que curar es un arte.

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# ARTICULOS ESPECIALES

## Schistosomiasis in the Dominican Republic: A Review

George V. Hillyer, Ph.D.

**Summary:** This report summarizes the available literature related to infection with *Schistosoma mansoni* in the Dominican Republic. Human infection is clearly present, but no estimate of prevalence or intensity of infection is available. Human cases have been documented in three foci in the eastern region of the Dominican Republic. These are Hato Mayor, El Seybo, and Higüey.

The present status of human infection with *Schistosoma mansoni* in Puerto Rico is presently unclear. The last comprehensive stool survey for schistosomiasis was done 30 years ago (reviewed in ref. 1). The most comprehensive prospective community-based study involved a small community in eastern Puerto Rico.<sup>2</sup> In spite of the absence of hard data it is widely thought that intensity of infection has decreased, although prevalence is unknown. In the past two years chemotherapeutic agents to treat human infection with *S. mansoni* have become available in Puerto Rico. This should result in a lowering of prevalence rates and of intensity of infection. This will make case finding by coprology increasingly more difficult and indirect serologic tests more important as a screening tool.

In neighboring Dominican Republic even less information is available. As a first step to develop strategies to detect infection a review of the available literature on this subject is presented in this report.

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### Background

When on May 1, 1851 Theodore Bilharz found in quantity white long helminths in blood from the portal vein of an Egyptian, he immediately recognized making a significant discovery. In his letters to Professor Siebold it is evident that he had discovered the blood flukes both in the intestinal veins and in "excrescences" in the urinary bladder. The eggs were oval and pointed toward one end. He also noted that the female worms in the urinary bladder were different from those found in the intestinal veins. The worms were named *Distomum haematobium*.<sup>3</sup> Fifty three years later I. González Martínez reported finding "*Bilharzia haematobia*" in two patients from Mayagüez, Puerto Rico, the eggs being found in feces, oval in shape, and with a subterminal spine.<sup>4</sup> This is what is now known as *Schistosoma mansoni*. In 1913, investigators at the Institute of Tropical Medicine of Puerto Rico, using an insensitive thin smear fecal examination, found 320 cases of schistosomiasis out of 10,140 patients (3.16%). Interestingly, one of the infected cases was "a patient coming from Santo Domingo".<sup>4</sup>

In the Dominican Republic, Read and colleagues at the Hospital San Antonio de San Pedro de Macorís found in 1924 eggs of *S. mansoni* in the feces of a patient who came from Antigua in the Lesser Antilles. That same year F.A. Defillo found *S. mansoni* eggs in the feces of a woman examined in Santo Domingo. Also in Santo Domingo, M. Pimentel Imbert visited the Laboratorio del Hospital Internacional de Ciudad Trujillo in 1938 and found *S. mansoni* eggs in a native sailor. This man, however, had lived in Caribbean islands known to be endemic for schistosomiasis (reviewed in 6, 7).

Thus although individuals in and from the Dominican Republic were known to be infected with *S. mansoni*, the source of the infection was unknown. No clinical studies were reported on these individuals.

### The First Autochthonous Cases

The first genuine case of schistosomiasis in a Dominican was discovered by Angel M. Ponce Pinedo on January 19, 1942. It was a 9 year old white schoolboy of Hato Mayor who came to the Outpatient Clinic of San Antonio Hospital in San Pedro de Macorís. During the next year and a half a total of six autochthonous cases were described, all residing in the region of Hato Mayor.<sup>8</sup> Fecal specimens obtained

from the patients were processed according to the qualitative, sedimentation-concentration method described by Hoffman et al.<sup>9</sup> Eosinophilia ranged from 8-30%. Hookworm was found in 5 of the 6 cases. The ages of the patients ranged from 9-23 years.

After the first case from Hato Mayor was discovered, Ponce Pinedo travelled to the town for the "purpose of interrogating the patient's family as to his habits, inspecting the streams in which he had bathed, and so forth. Accordingly, he was told that the patient used to bathe daily in a small creek called "Pañe-pañe," which empties during the rainy season into another stream called "Las Guamas", both of which flow very close to town. Ponce Piñedo collected numerous, large *Biomphalaria glabrata* snails from those streams and was able to demonstrate that 5% of them shed forktailed cercariae suggesting that they were *S. mansoni*. Infection of rabbits resulted in the development of adult worms.<sup>8</sup>

In that original report the summary states abruptly that the "number of infected persons found to date reveals a percentage of 0.27 among a total of 4,500 whose feces were examined".<sup>8</sup> This comes out to be 12 infected persons. The fact that all of the infected patients were young (9-23 years old), and assuming that older age groups were examined, suggests that the endemic focus was of relative recent vintage.<sup>6</sup> Ponce Pinedo's thesis<sup>10</sup> reprinted as a collection of his writings in 1976 is fascinating reading.<sup>11</sup>

In summary, then, by 1943 it was clearly established that there existed a focus of human schistosomiasis in Hato Mayor with the presence of *Biomphalaria* snails shedding fork-tailed cercariae which after penetrating the skin of rabbits develop into *S. mansoni* adult worms.

### Studies in the 1950s

The next significant study was reported by Olivier et al., who surveyed the Hato Mayor area in 1951.<sup>12</sup> They also found *B. glabrata* snails in the two connected streams (Las Guamas, Paña-Paña) on the eastern margin of the town and confirmed by infecting mice that the cercariae shed by the infected snails were *S. mansoni*. No *B. glabrata* snails were found in other streams up to 20 kilometers from the town of Hato Mayor leading the authors to conclude that the snails host for *S. mansoni* appeared to have a very restricted distribution in the vicinity of Hato Mayor. They also obtained stools from 243 children from Hato Mayor and between the ages of 5 and 15 inclusive, and processed them by an acid-ether concentration method. *S. mansoni* eggs were found in 52 or 21.4% of the stools examined. Thus the authors concluded that a serious endemic focus of schistosomiasis *mansoni* existed in the vicinity of Hato Mayor and that the disease was being acquired by a relatively large proportion of the children of the town. Since the endemic area was apparently restricted to narrow geographic limits they considered this especially suited for a study on the use of snail control by chemical means.

Thus in 1952 Vaughn et al.<sup>13</sup> found that a single application of sodium pentachlorophenate essentially wiped out the *B. glabrata* snails from Las Guamas and Paña Paña streams. They also noted destroying a lot of fish and shrimp and that lesser amounts of the chemical were required to kill these animals than snails.

However, additional snail foci were evident in nearby areas at that time. J. de Oliveira Coutinho from Brazil, in an unpublished report done in 1952 and cited by Ponce Piñedo<sup>11</sup> found infected *B. glabrata* snails in Manriquez stream and water pools near the road east of Hato Mayor leading to El Seybo. He also examined stools samples of 653 children and adults from Hato Mayor, finding a 15% prevalence rate. Of special interest is that he also examined 65 stool samples from adults and children from Las Palmillas, a rural area 4 km from Hato Mayor, and found 4.5% infected with *S. mansoni*. The finding of 2% of the *B. glabrata* snails shedding cercariae (presumably *S. mansoni*) in water pools near the road from Hato Mayor to Las Palmillas further supports the notion in 1952 that infection with *S. mansoni* was prevalent in a population other than Hato Mayor and that this may have been a new focus of transmission.

### Studies in the 1960s

Since the studies done in the early 1950s, little else is documented until late in the 1960s. However, in 1962, with Dominican health officials, Maldonado<sup>15</sup> performed intradermal skin reactions following the method of Kagan and Pellegrino<sup>16</sup> on 175 schoolchildren from the Hato Mayor region finding 30% positive reactors (46% in males, 16% in females). Children less than 10 years old had 19% positive reactors. Among those 10-11 years old prevalence of positive reactors was 32%. In addition, 14 of 32 *Biomphalaria* snails collected in the region were sheddings *S. mansoni* cercariae. In another survey, 172 male orphan children in Santo Domingo were tested by the intradermal reaction and 25.6% were positive reactors. Interestingly, 67.5% of those positive had a history of fresh water contact in the capital city as well as other unspecific locations. Finally, some positive reactors by the intradermal test were found in the province of Valverde in the northwest region of the Country, although no results were presented.

Ponce Pinedo reports<sup>11</sup> that in 1965 of 167 stool samples examined from children of 8-13 years old from Hato Mayor 31% had *S. mansoni* eggs.

In 1968 the Secretaría de Estado de Salud Pública y Asistencia Social (SESPAS) held a "Simposio sobre la bilharziasis en Santo Domingo" (reviewed in 17) in which local investigators and outside consultants reviewed the status of schistosomiasis in the Dominican Republic. It was significant in that a recommendation was made to form a National Committee for the Eradication of Schistosomiasis.

Etges and Maldonado briefly reviewed the status of schistosomiasis in the Dominican Republic, with special emphasis on its intermediate host, and biological control with snail competitors.<sup>18</sup>

### Studies in the 1970s

The 1972 Anonymous monograph by SESPAS<sup>15</sup> is a fascinating document. In it is a statement on how Dr. Ponce Pinedo thought schistosomiasis was introduced into the Dominican Republic. It was a Puerto Rican named Tello Zapata. According to local gossip at Hato Mayor, Tello Zapata cultivated a vegetable garden in his property near the Paña-Paña stream. When he died the people said it was because of schistosomiasis and called it "enfermedad de Tello



Zapata". This, of course, was in the 1940's, when the first autochthonous cases were described.

In May, 1970 a schistosomiasis control center was formally inaugurated at the Hato Mayor Health Sub Center with Dr. Rafael Brugal Montolla as its first Director. Control efforts included education of the population, the pacing of signs by the streams warning the citizens of the danger of infection, biological control using *Marisa cornuarietis*, and chemical control of snails first using Bayluscide, later Frescon. Beginning in 1971, individuals found infected by fecal examination (Hoffman sedimentation concentration method) were treated with a single dose of hycanthone (Etrenol). Previously, they had been utilizing stibophen (Fouadin).

There is a reputed report by Brugal Montoya dated 1979 and titled "Informe anual sobre 8 años de labor del Centro de Erradicación de la Bilharzia, Archivos S.E.S.P.A.S., Dirección de Epidemiología," and cited in reference 19. A visit to S.E.S.P.A.S. by the author in July, 1982 resulted in failure to obtain a copy of this report. Additional efforts by Mercedes Vargas, from UASD, to obtain this report were unsuccessful. However, the report is cited by Sánchez Limardo and Grullón Pérez<sup>16</sup> and is extracted in the next paragraph and Table.

In 1972 and 1973 two new areas of *S. mansoni* transmission to humans were found. These were in Higüey and El Seybo.<sup>19</sup> The transmission areas were located and, as in Hato Mayor, chemical snail control was applied. All detected positive human cases were treated with hycanthone. If one notes the first year of data for each area summarized in the Table (1970 for Hato Mayor, 1972 for El Seybo and Higüey) the highest case finding was during that first year. Assuming that all of the detected cases were treated, then chemotherapy had a dramatic impact in lowering the infected population. It is difficult to make firm conclusions, however, because snail control and education were concurrent ongoing efforts. (It should be noted that the 1974 figures for El Seybo are unrealistic as a small sample of cases was examined. However, during these same periods, near 100% cure rates were being reported). Whichever way the results are examined, it is obvious that a

precipitous drop in human *S. mansoni* infections was observed. However, even these conclusions are suspect because the criteria for selecting the individuals for stool examination are unknown and no follow-up information on the treated individuals is provided.

With such apparently low prevalence rates found, direct parasitologic case finding by an insensitive, qualitative test such as is the Hoffman assay becomes more difficult.

In order to improve case findings, Mercedes Vargas used the intradermal reaction with *S. mansoni* adult worm antigen extract, testing for reactivity 200 children 3-12 years old and 124 youngsters 12-20 years old in El Seybo finding 17% and 28%, respectively, positive reactors. In Higüey, 200 university students also were tested for skin test reactivity and 23.5% were positive reactors. Twenty of the positive reactors were examined for *S. mansoni* infections by rectal biopsy and 19 were positive.<sup>21</sup> These tests were done in 1972 and demonstrate that prevalence of human infections with *S. mansoni* at that time was certainly higher than that reflected in the Table of this review in which the Hoffman sedimentation concentration method was utilized.

The above review on the status of schistosomiasis in the Dominican Republic suggests that human infections exist. However, no estimate of prevalence is presently available. Since 1980, individuals identified as infected with *S. mansoni* at the Hato Mayor Public Health Sub-Center have been treated with a single oral dose (15 mg/kg) of oxamniquine (Mendez Silfa, personal communication).

Efforts should be directed to a limited survey of the three areas already determined to have a human population infected with *S. mansoni*. These are: Hato Mayor, El Seybo, and Higüey. For example, a survey carried out in 1975-1976 in and around La Romana in which over 20,000 stool samples were examined (Hoffman sedimentation concentration method) only 8 persons infected with *S. mansoni* were detected and all were from Higüey.<sup>19</sup> Thus schistosomiasis in the Dominican Republic appears to be focal in nature and a population based survey to determine prevalence for schistosomiasis in those three areas could be made at reasonable cost.

TABLE

Prevalence rates of human infection with *Schistosoma mansoni* detected by the Hoffman sedimentation-concentration method in three areas of the Dominican Republic.

YEAR	HATO MAYOR			EL SEYBO			HIGUEY		
	Cases Examined	Number Positive	%	Cases Examined	Number Positive	%	Cases Examined	Number Positive	%
1970	3,028	328	10.8						
1971	4,173	137	3.3						
1972	4,174	88	1.9	1,228	60	4.9	4,596	560	12.2
1973	7,668	97	1.3	3,957	58	1.5	8,534	216	2.5
1974	6,261	53	0.8	217	22	10.1	6,373	60	0.9
1975	6,455	23	0.4	9,284	3	0.03	14,517	50	0.3
1976	5,361	12	0.2	644	0	0.	4,974	56	1.1
1977	5,570	14	0.2	5,427	29	0.5	3,820	29	0.8
1978	3,989	16	0.4				3,285	14	0.4

**Resumen:** Este artículo resume los trabajos publicados relacionados a infección con *Schistosoma mansoni* en la República Dominicana. Se han documentado infecciones humanas, pero no existen encuestas en las que se le pueda estimar la prevalencia o intensidad de infección. Las infecciones humanas documentadas provienen de tres áreas en la región este de la República Dominicana: Hato Mayor, El Seybo e Higüey.

### Acknowledgements

The investigations of the author are supported primarily a grant from the Edna McConnell Clark Foundation and by NIH Grant No. RR-8102-11. The help and encouragement of Dr. Norman Maldonado and Dr. Lillian Haddock at the UPR Medical Sciences Campus to do the present study is gratefully acknowledged. The assistance of Mercedes Vargas (Director of the Instituto de Investigaciones en Bilharzia, Universidad Autónoma de Santo Domingo) in obtaining some of the references is warmly appreciated.

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# Medicando al Deprimido

Víctor Bernal y del Río, M.D.

**Resumen:** El articulista discute depresión y ansiedad, síntomas psicológicos más frecuentes en la práctica. Insiste en estipulaciones necesarias para examen. Hace acopio de diferenciación y señala el uso de fármacos sin extenderse en especificación enumerativa de antidepresivos o angiolíticos cuya lista y dosificación puede leerse en cualquier armamentarium terapéutico. Señala la necesidad de atenerse a dosis suficientes y abunda en la existencia de la disciplina con el paciente deprimido. No cita en su artículo qué recetar al deprimido, si no cómo recetarlos. No con que tratarlos, sino cómo tratarlos. Incluye el manejo del problema enorme de los efectos secundarios de las medicaciones en pacientes dados en abundar y con determinado doblez hipocondríaco.

La depresión es hoy por hoy, juntamente con la ansiedad, el síntoma psicológico más frecuente de la práctica. Es labor primordial de diagnóstico la separación de ambas entidades y cuando aparecen juntas, la estipulación del por ciento de angustia y/o depresión que aqueja al paciente. Más que hablar de depresión vamos a hablar de deprimidos, así como también en lugar de hablar del suicidio, hablaremos del suicida; en lugar de insomnio, hablaremos de los insomnes. Triade esta: **Depresión, Insomnio y Suicidio**, de máxima importancia en el manejo de estos pacientes. El deprimido, contrario a lo que generalmente se cree no es un triste, sino un enojado. Su queja más que quejumbrosa es quejosa y litigante. Utiliza y exhibe el escapulario de su depresión para salvarse de seudoculpas por las cuales se castiga continuamente. Inferimos de esto que el "¡ay bendito!", la compasión, y la simpatía no forman parte del armamentarium terapéutico.

Óptima labor se obtiene separando la depresión pura (muy rara) de las mezclas que tan frecuentemente observamos en la práctica. La depresión pura debe evaluarse por la concordancia de depresión, lentitud del pensamiento y en la expresión de las ideas y lentitud psicomotriz. Triade esta que debe ser armoniosa y concordante en su intensidad. Estipulada, la depresión pura debe evaluarse por su intensidad entre moderada, simple e intensa. Las dos primeras modalidades, pueden ser manejadas en consultorio hoy. La tercera es modalidad que debe plantear la decisión de hospitalización. En las depresiones puras, sean éstas simples, moderadas o severas, la exploración de ideas suicidas es imperativa y su ausencia puede catalogarse como mala-práctica-médica. La idea suicida siempre se explora en el paciente deprimido

con preguntas aclaratorias de fantasía suicida, modalidad, historial de intentos, seriedad de los mismos, posibilidades de acción y de manejo preventivo. La prevención empieza por la exploración directa y clara por parte del médico. No implantamos ideas suicidas en nadie, así como no implantamos ningún tipo de idea; las desenterramos, las descubrimos, hacemos posible que el paciente las exprese, recibirlas sin aspavientos ni misericordia es la primera labor terapéutica, pues que, secreto entre dos, compartido sin escándalo, es menos peligroso, menos se acerca a la consumación. Aquí no reza el dicho de Sancho: "En casa del ahorcado no menciones la sogá." Muy por el contrario en la mente del que está conjeturando y obsesionado con la idea suicida, la apertura de una puerta de escape con la pregunta certera hace menos probable que la sogá sea usada.

La depresión es síntoma que se presenta o puede presentarse acompañando todas las entidades nosológicas de la práctica psiquiátrica y médica. Acompaña todas las neurosis, la esquizofrenia, los síndromes cerebrales crónicos, etc. En la práctica de oficina, para diferenciar, debemos simplemente atender a las expresiones de angustia directa y a las expresiones de queja depresiva. A la depresión pura la acompaña un lentitud en el pensamiento y disminución en la expresión de ideas, nos sorprende pues el paciente modelo que alegando estar deprimido procede a una hemorragia verbal de relato, queja, evolución, historial, detallismo que muchas veces cubre la casi totalidad de la primera entrevista. Como la decisión medicamentosa ha de ser distinta y a veces conflictiva, la evaluación de depresión vs. angustia es de suma importancia. Nos ayudan a esta aclaración el estudio del historial de dormir, insomnios matinales o de madrugada versus insomnio de prima noche, la concomitancia de los síntomas neurovegetativos, apetito sexual-social y alimentar disminuidos, estreñimiento, centralización del discurso en la queja e historial evaluativo de la personalidad y brotes anteriores. Expresa atención debe darse a las quejas somáticas que acompaña la queja depresiva, manejo este que ya nos obliga a uso de nuestros conocimientos de dinámica. La queja somática puede o no ser el síntoma de presentación. Debe estudiarse si pertenece exclusivamente a alguno de los sistemas cardiorespiratorios, digestivos, etc., o si mezcla sistema inadvertidamente. Las quejas que verdaderamente mimetizan cuadros clínicos conocidos con confusión diagnóstica, se ven frecuentemente al examinar personas que, en una forma u otra, están relacionadas con la práctica médica, o personas que por su capacidad intelectual general tienen conocimiento de entidades nosológicas. Nos extendemos en estas consideraciones toda vez que el médico debe decidir rápidamente si envía al paciente para exámenes de laboratorio, si se entretiene extensamente en exploración interesada de la sintomatología, si repite dicha exploración consistentemente, lo que puede dar al traste, precisamente, con su labor de manejo del deprimido. La exploración detallada, repetida e insistente, la reevaluación sin límites puede ayudar a una fijación hipocondríaca que será más tarde muy difícil de extirpar. En términos generales, el médico debe acostumbrarse a oír la queja, evaluarla en silencio y no responder activamente a la misma. Comprendo la sorpresa que estas declaraciones pueden tener en cada uno de ustedes —ya que va en contra de la fibra misma de la práctica médica. Es, sin embargo, cierto que algunos entretenimientos de repetición de relato, de quejas, evitan que se use el tiempo de la entrevista para la exploración y expresión de problemas psicológicos.

gicos del paciente. Es reparto indebido y erróneo del tiempo y del oído del médico la seudopaciencia al oír y dar pábulo a la queja hipocondríaca, amén de terminar, eventualmente, con impaciencia malamente escondida.

Debe explorarse siempre al evaluar pacientes levemente deprimidos el uso por los mismos de medicación antihipertensiva, recientemente estipulada, cambio de dosis, o cambio de medicación. Manejo que hará necesario la comunicación con el internista a cargo del paciente. Evaluada la depresión en cuanto a su pureza, su intensidad y su mezcla con la angustia y otros síntomas psicológicos, tomando en consideración, como dije antes, historial de insomnio, expresión de queja hipocondríaca, fluidez en el relato e insistencia de la queja; debe procederse hoy básicamente a una decisión sobre la siguiente tetralogía.

1. Manejo del insomnio con hipnóticos.
2. Manejo de la ansiedad con medicación tranquilizante.
3. Manejo de la depresión con antidepresivos.
4. Psicoterapia.

El insomnio de madrugada no es indicación para medicación anti-insomnio. El insomnio de prima-noche si no incluye un cambio en el reloj del dormir ni cede a ésta, esto es, personas insomnes hasta la una o las dos de la madrugada, pero que duermen comunmente hasta las nueve, o que se rehabilitan en siestas extensas no deben ser medicadas. En los casos, pocos, de insomnio de prima-noche con reducción vasta de las horas de sueño —sin siesta prolongada, puede requerir de emergencia por muy poco tiempo una cantidad limitada de medicación hipnótica. El verdadero problema de los pacientes combinados (ansiedad-depresiva) es que el uso de medicación tranquilizante al mejorar y reducir las expresiones de ansiedad aumentan por el contrario la depresión y puede entrar al armamentarium medicamentoso en situación de noria-perpetuante. En términos generales, aconsejo reducir al máximo la medicación tranquilizante y descansar en el conocimiento de que la medicación antidepresiva —si sostenida en dosis suficientes— eventualmente aclarará ambas sintomatologías. La tendencia es a lo contrario —aliviar la angustia de toda costa— ambas (la del médico y la del paciente) y considerar la depresión como el síntoma “target symptom”.

Todos nosotros estamos conscientes del apareamiento de potentísimas drogas psicotrópicas específicamente utilizables en la depresión. El apareamiento último de combinaciones variadas de antidepresivos y tranquilizantes, de cambios en el uso de tricíclicos, inhibidores de las aminozidadas, carbonato de Litio, etc., en intento de panacea para todos los casos. También estamos conscientes de las prédicas constantes de la literatura en el uso de dosis adecuadas (altas), uso prolongado antes de apareamiento de mejoría, dosis de mantenimiento, evaluaciones periódicas, titraje de algunas, exámenes de laboratorio, pruebas de riñón, de hígado, peligros hipotensivos, etc., y, finalmente, el gran “cuco” de los efectos secundarios que en Inglés llaman “por el lado” (side effects), y que nadie verdaderamente sabe qué hacer con ellos. ¿Qué médico no se ha sentido consternado al leer con cuidado la cantidad de avisos, advertencias, precauciones y efectos inesperados que contiene la literatura de los productos que utiliza diariamente? En la práctica, sin embargo, observamos caso tras caso en que

pacientes debidamente diagnosticados, utilizando la medicación indicada, piden consulta y van de médico en médico por ausencia de mejoría esperada. Las causas son siempre las mismas: (1) Uso indebido de dosis, o se le ha recetado dosis baja o el paciente ha manejado la dosificación y se ha mantenido en dosis baja; (2) El paciente (deseperado), suspende la medicación tempranamente, la cambia a su antojo, la toma a su conveniencia y la reporta o informa a su conveniencia también. Estas maniobras del paciente deprimido son parte de la dinámica de su enfermedad y es menester que el médico que lo trata esté consciente de los mismos para prevenir, evitar y conseguir resultados decisivos. Me repito, el paciente deprimido es un enojado, un cachorro, un desobediente, un agresivo, un rabioso, sentimientos estos de los cuales él no está consciente de ellas. Pero su comportamiento, debidamente interpretado, nos lo señala.

*Desobediencia de dosis:* El paciente deprimido tiende a reducir dosis, a cambiar horario, a manejar la terapéutica a su antojo con razonamientos y racionalizaciones de falta de resultados, intensificación de síntomas, aparición de sensaciones extrañas, recrudecimientos de quejas antiguas que culminan en negarse rotundamente en algunos casos a la continuación del uso de la medicación o de la visita al médico. Familiares poco avezados y a veces compañeros bien intencionados, responden a esta maniobra con complicidad en intento de complacencia, de engraciar y en duda misma de la eficacia terapéutica de su intervención. Acostumbro de comienzo, hacer estipulaciones precisas de dosis, de horario fijo que comunico con seriedad y sin miramientos al paciente directamente no importa cuán lloroso o quejoso esté el mismo. Tiendo a dosis altas, rápidamente ascendentes y estipulo uso mínimo de tres semanas para el apareamiento de mejoría evidente. Me reporto para mi evaluación a evidencia de mejorías indirectas el insomnio, el apetito, etc., haciendo caso omiso del recrudecimiento o intensificación de la queja. Considero las ausencias de disciplina como expresión específica del enojo que aqueja a estos pacientes a agresión velada de la autoridad del médico o indisciplina racionalizada, a intento inconsciente de continuar en la miseria de su situación para allegar a sí mismos el perdón buscado por flagelación constante, que necesita para remediar faltas reales o imaginadas. En el tratamiento de estos pacientes el “ay bendito” es una discordancia. Entrego a la mano recetas, direcciones precisas y cuentas, estipulo la realidad de la disciplina de horario, recibo directamente pagos y observo firmeza en mis declaraciones de manejo sin extensión en expresiones de optimismo tranquilizante. No están indicadas. Preferiblemente dicto al paciente las estipulaciones de dosificación y horario, citas próximas y demás especificidad de la relación. Repaso con ellos para aclaración. Entrego a la mano recetas y recibos, con esto quiero decir que no los pongo sobre la mesa para que el paciente los tome. Si el paciente pone su cheque o dinero sobre la mesa lo recojo en su precencia. En visitas próximas repaso decisivamente el alejamiento de dosis, la posposición de toma, el olvido y señalo sus consecuencias. Me repito, como todo síntoma psicológico, el deprimido agarra y se ampara en su depresión y no quiere cortarla. No importa las protestas en contrario. El síntoma psicológico es la solución que ha utilizado, le pertenece, desea continuarlo y ve cualquier intento terapéutico como un asalto al síntoma que le pertenece y por lo tanto como un asalto a la integridad de su ente psicológico.

Clásicamente el médico escribe recetas y ordena tratamiento al terminar la entrevista antes del paciente marcharse.



En el tratamiento del deprimido esta práctica clásica debe sufrir modificaciones.

Saludo, interrogación sobre el resultado de la medicación, mejorías, efectos secundarios, examen, recetas, etc., deben revisarse. Recetas, explicaciones, órdenes, prohibiciones, modos de administración, etc., deben situarse en el medio de la entrevista para permitir al paciente expresarse sobre los mismos. Esto hace posible también el cierre de la entrevista a tiempo sin el apareamiento de preguntas vitales sobre dudas al terminar la entrevista, obligándonos a su prolongación. Con un paciente deprimido hago especificaciones de dosis, nunca digo "tres o cuatro pastillas, cuatro o seis pastillas..." o "puede tomarlas según sea necesario", aún con la medicación para el insomnio.

A pesar del adelanto monumental en el tratamiento de los drepresivos con el apareamiento de la medicación antidepresiva, todos los autores concurren en que la combinación de psicoterapia con la administración de medicamentos es el tratamiento de preferencia. La literatura es conteste en esta conclusión. Innumerables autores se han ocupado de la combinación de psicoterapia y farmacoterapia. Sin embargo, cabe señalar que, a pesar de aceptarse lo anteriormente estipulado: combinación de psicoterapia y farmacoterapia como tratamiento de referencia, en la mayoría de la práctica y especialmente en los servicios públicos, un instrumento terapéutico sustituye lentamente al otro, esto es: se descansa la mayor parte del tiempo en servicios orientados a dar medicamentos con entrevistas de quince y a veces de cinco minutos. Las clínicas se tornan en dispensadoras de recetas y repartidoras de pastillas, a veces, al bulto. La entrevista de 50 minutos tan vilipendiada se reduce a 15 y se gradúa de cinco. No se puede hacer psicoterapia en cinco ni en quince minutos. No importa la capacidad, el entrenamiento, la dedicación, el entusiasmo, o la ignorancia, el conocimiento, la experiencias del terapeuta. La psicoterapia necesita el tiempo. En la combinación de psico y farmacoterapia el tiempo estipulado de entrevista, duración y programa, sigue siendo la forma de proceder del médico.

He dejado para el final la discusión de los efectos secundarios o efectos de lado (side effects), como los llaman los americanos. La práctica de la medicina actual vive una esquizofrenia científica. Por un lado los temores omnipresentes de los litigios de (mal practice), y los fondos de compensación. Por otro lado la "buena ética y práctica de la medicina" practicable. El médico vive entre la lectura y el conocimiento de los aterradores "warnings" de la literatura de cada producto, de la enumerativa interminable de las posibilidades de efectos secundarios; algunas de peligrosidad importante. Las recomendaciones y preferencias, exámenes múltiples, continuos, la carestía de los mismos, la ineficacia de algunos, las complicaciones de otros, etc., y entonces, ¡pobre mortal! debe decidir sobre una práctica plausible. Aún en medicamentos que utilizamos por largo tiempo, al releer la literatura de los mismos, en ocasiones variamos de la sonrisa incrédula al temor atisbante. Con cada medicación nueva nuestra inseguridad se agiganta ya que son lanzadas al mercado con tales objeciones que no se sabe cómo dar comienzo a su uso. Pasados los años se aplacan las ansiedades, se usa el medicamento con seguridad, y extrañamente parece que los tales efectos secundarios se hacen menos evidentes, más leves, menos frecuentes y varían de una comunidad a otra, extrañamente. Cabe preguntar si en parte algunos efectos secundarios no son expresión por el paciente y provocación por el experimentador al escribirse ese capítulo difícil de la medicina experi-

mental que incluye, inevitablemente, el uso de humanos con las inseguridades propias de la experimentación. De todas maneras el médico enterado, avezado a los peligros inherentes en el uso de la medicación, tenderá a quedarse en pocas dosis, a reaccionar en demasía a las reacciones de cada paciente y a informar extensa y expresamente con detalles sobre todos y cada uno de los posibles efectos secundarios de la droga. Debe aliviarnos la ansiedad pero no desaparece el conflicto en la legislación que hace obligatoria la inclusión, en cada paquete, de un medicamento —de una exposición total de lo que se conoce sobre ese medicamento incluyendo todas las posibles reacciones negativas.

Nos toca decidir y tal decisión debe hacerse con conocimiento y uso de la dinámica de la depresión, salvo ligera mención de la sequedad de la boca que va a aparecer con el uso de los medicamentos antidepresivos. Suelo ser parco en mis explicaciones en mi mención de los mismos so pena que se implanten en la psiquis del paciente, crezcan desafortadamente, alimenten la queja hipocondriaca, la sostengan, la razonen y la mantengan eternamente. No tengo que explicar, desde luego, a esta audiencia las realidades de complicaciones posibles en algunos casos específicos de falla renal, dificultad cardiopulmonaria, reacciones tiroideas, etc. con algunos medicamentos más específicamente en el tratamiento de las reacciones depresivas bipolares con carbonato de Litio.

Al aparecer mención —como generalmente aparece por el paciente— del efecto secundario evidente con el medicamento debe escucharse con atención, sin aspavientos. Interesantemente en pacientes en dosis de mantenimiento de larga duración, revierten éstos a silenciar completamente la mención evidente de sus incomodidades secundarias al uso del fármaco (estreñimiento, descensos de la libido, aumentos de peso, retención de agua, etc.), y es necesario que el terapeuta los explore e investigue para intentar ponerles remedio. Sigue luego su curso la psicoterapia prolongada necesaria y dinámica.

# Carta del Presidente de la Cámara de Delegados de la Asociación Médica de Puerto Rico

## NECESIDAD DE AGENDA PARA LA ACCION

**L**os cambios en el área de servicios de salud, especialmente aquellos motivados por sistemas de pagos por los servicios, han sido dramáticos en los últimos años. Estos cambios se reflejan en un sinnúmero de nuevas siglas D.R.G., P.P.O., I.P.A., P.R.O., P.H.P. ¿De cuántas sabes su significado? Tu contestación te confirmará que están habiendo cambios acelerados. El ambiente que nos rodea es distinto y sobre todo amenazante a la práctica de la Medicina como la hemos conocido.

El Gobierno está estimulando la competencia para tratar de reducir costos. Esta medida, alegan, va en sustitución de la Reglamentación Federal. Sin embargo, la evidencia está aumentando de que estaremos atrapados entre el estímulo de la competencia y el posible resurgimiento de Reglamentación Federal. Estas fuerzas están atrapando a los médicos entre los Hospitales, que están tratando de utilizar los médicos como empleados, las ciudades, que al tratar de bajar costos están negociando directamente con grupos de médicos, los H.M.O.'s empleando médicos a sueldo fijo y la industria utilizando los P.P.O. (preferred provider organization). Estamos atrapados unos contra otros al tratar de competir por sobrevivir en un ambiente, donde ya hay una sobre oferta de médicos.

Las fuerzas externas nos están separando y poniéndonos unos contra otros. Es fundamental que resolvamos nuestras diferencias internas, aumentando la participación genuina, guiándonos por nuestro reglamento y apoyando el liderato no comprometido con otros intereses que no sean los de la Asociación Médica de Puerto Rico. Tenemos que rechazar el liderato autocrático, al igual que aquél que apoya la anarquía, la no participación como estrategia para lograr sus propósitos. Necesitamos, más que nunca de un liderato democrático y libre que haga de nuestra Asociación una Institución libre para poder luchar por la excelencia de la práctica de la Medicina, según la vemos los médicos de mente libre que creemos firmemente en nuestro sistema democrático de vida.

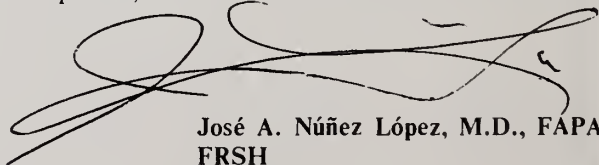
Tenemos que reevaluar los mecanismos financieros de nuestra Asociación Médica, los servicios que ofrecemos a nuestros miembros y la calidad de nuestra participación en el establecimiento de política pública de salud en nuestro país. Urge el que apoyemos aquellas medidas que fortalezcan nuestros recursos económicos, pero parte de estos recursos tendrán que ser asignados a un estudio práctico de nuestra

situación ante los retos, aparentemente imposibles de vencer, que se nos están presentando y se nos presentarán en los próximos años. Nuestra Asociación no puede seguir dependiendo en forma tan directa y exclusiva de las cuotas de los médicos. Urge el que los instrumentos con que contamos en nuestro Reglamento se agilicen, para que logremos un plan de acción que nos permita, en los próximos años, contar con un sistema financiero estable que pueda aumentar nuestros recursos a la medida de nuestra necesidades y que no sea oneroso a nuestros miembros a través de las cuotas. Sin embargo, para poder iniciar estos logros tendremos que todos, como miembros de la Asociación Médica, como miembros de los distritos, contribuir al máximo de nuestros medios para poder salvar a nuestra Asociación de la situación fiscal difícil en que se encuentra, y a la vez pedir que se tomen las medidas que garanticen que este problema no se seguirá repitiendo.

Tenemos que hacer una agenda para la acción. Tenemos que mirarnos a nosotros mismos y al ambiente cambiante que nos rodea. El ambiente cambiante de la medicina, de las nuevas realidades económicas, de los cambios que están ocurriendo en la forma de pensar de los médicos jóvenes, que están asumiendo liderato en nuestra sociedad y del enfoque gubernamental nuevo de financiamiento de los servicios de salud.

La Asociación Médica y todos sus distritos van a tener que reevaluar su forma de funcionar, su financiamiento, sus recursos disponibles, para lograr sus objetivos y desarrollar un plan, una agenda de acción para los próximos años que nos permita, no solamente sobrevivir, sino influir efectivamente en el diseño del futuro de la práctica de la medicina en Puerto Rico.

El reto es grande y sólo una Asociación libre, unida y fuerte podrá confrontarlo exitosamente. El compromiso es, y tendrá que ser, de todos



José A. Núñez López, M.D., FAPA,  
FRSH  
Presidente  
Cámara de Delegados

4 de marzo de 1983





## PATHOLOGY *Review*

María Castillo, M.D.

Una mujer de 25 años con historia de haber recibido radioterapia al área del cuello a la edad de 10 años, presenta un nódulo en el lóbulo derecho del tiroides. La determinación de  $T_4$ ,  $T_3$  y TSH son normales. Calcio 9mg%. El escintigrama del tiroides utilizando  $I^{123}$  reveló un nódulo frío. El paciente fue sometido a cirugía.

¿Cuál es su diagnóstico?

- a. Adenoma folicular del tiroides
- b. Hyperplasia adenomatosa difusa del tiroides
- c. Carcinoma medular del tiroides
- d. Carcinoma papilar del tiroides
- e. Quiste intratiroideo

### Carcinoma Papilar del Tiroides

Es el más común de los tumores malignos del tiroides con una incidencia aproximada de 70%. Ocurre a cualquier edad particularmente entre los 30 y 40 años. Es el tumor maligno del tiroides más frecuente en niños y la causa más común de agrandamiento nodular del tiroides en niños en los Estados Unidos. El tratamiento con radioterapia al cuello en la niñez es un factor etiológico comprobado.

El carcinoma papilar del tiroides puede presentarse clínicamente como un nódulo "frío" solitario en el escintigrama. En ocasiones la primera manifestación clínica es un ganglio linfático metastático a la región del cuello. Las pruebas funcionales del tiroides son normales.

### Patología

Es un tumor que varía de blando a firme. Tamaño promedio de 2 centímetros de diámetro. Bordes pobremente definidos o a veces encapsulado. Puede ser multicéntrico con varios nódulos o focos en ambos lóbulos del tiroides. (Fig. 1) El patrón histológico es papilar, pero casi todos presentan áreas foliculares. Los cuerpos de psamoma son focos pequeños de calcificación que aparecen con frecuencia en carcinomas papilares. (Fig. 2)

Estos tumores tienden a diseminarse por vía linfática a la región cervical y mediastínica.

El tratamiento es quirúrgico. El yodo radioactivo es generalmente poco efectivo a menos que no se demuestren metástasis foliculares funcionantes.

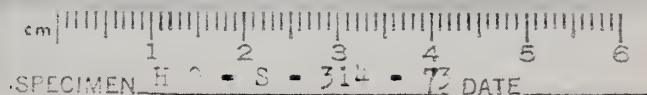
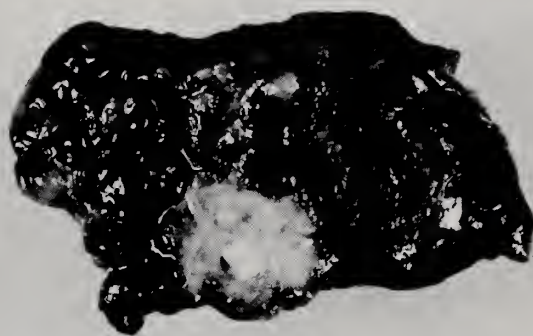


Fig. 1: Carcinoma papilar del tiroides. El tumor es gris, firme, no encapsulado y mide dos centímetros de diámetro.

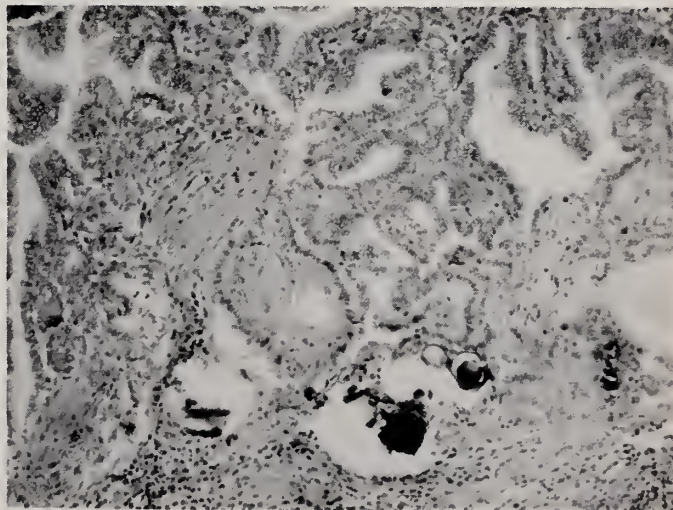


Fig. 2: Carcinoma papilar del tiroides. El tumor consiste en frondas tapizadas por células cuboidales de núcleo hipercromático. Cuerpos de psamoma característicos aparecen en la parte inferior de la fotografía.

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# Sonography Quiz

Rafael M. Rivera, M.D.

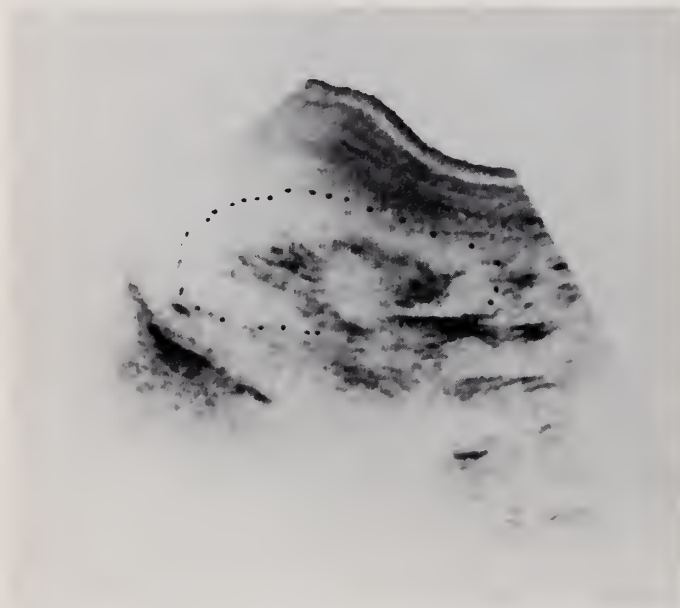


Figure A: Sonography right kidney, longitudinal section.

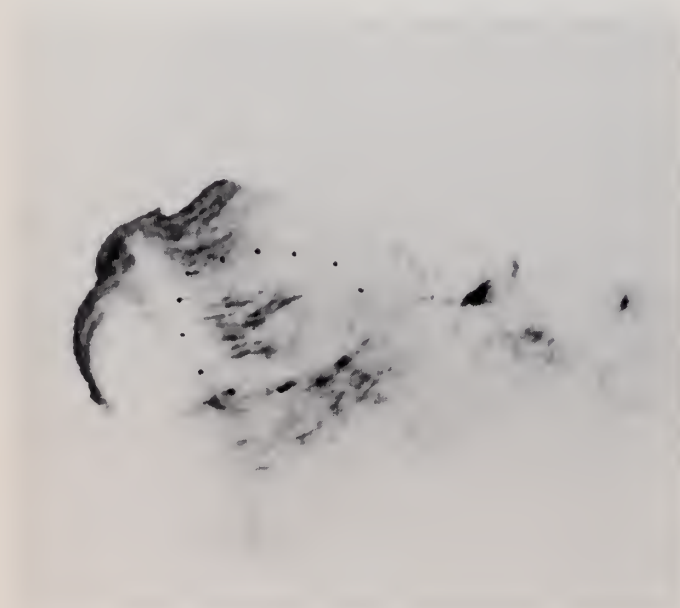


Figure B: Sonography right kidney, transverse section.



Figure C: Excretory urography

The above sonographic images are longitudinal (A) and transverse (B) sections of the right kidney. The patient was a 50 years old male with right flank pain and hematuria. The most likely diagnosis is:

- A. Renal cell carcinoma
- B. Renal sinus lipomatosis
- C. Transitional cell carcinoma
- D. Hydronephrosis
- E. Renal pelvic staghorn calculus

**Correct diagnosis: C. Transitional cell carcinoma**

## Discussion

The sonographic sections shown demonstrate a roundish mass just in the hilus of the right kidney. Excretory urography (fig. C.) clearly showed a polypoid tumoral mass identified as a filling defect inside the right renal pelvis.

Transitional cell carcinomas are the most common primary renal pelvic tumors. Occasionally, squamous cells and very rarely adenocarcinomas are seen. Sonographically, these tumors are manifested as low level echogenic masses separating the strongly echogenic central echo complex of the renal sinus. The echogenicity of these lesions is quite similar to that of the normal renal cortex and, thus, must be differentiated from duplicated collecting systems and from



post-inflammatory cortical hypertrophy (Bertin Columns). Renal sinus lipomatosis presents sonographically as a diffuse increase in the renal central echo complex and hydronephrosis manifests as multiple cystic spaces in the renal sinus. Renal cell carcinomas may present sonographically as solid, or, less frequently, as partially cystic masses. Fortunately, these lesions, although may involve the renal sinus, are usually cortical in location causing a deformity of the peripheral renal contour and are easily differentiated from central pelvic lesions.

Transitional cell carcinomas are usually first suspected from an excretory urogram. Sonography is then indicated to further document the diagnosis since non-opaque renal pelvic calculi or blood clots may simulate a renal pelvic tumoral mass on urography. Pelvic stones will be strongly echogenic at sonography and will cast a well defined acoustic shadow. The echogenicity of blood clots will vary depending on the organization of the clot and it's size will change in close follow up studies. With excretory urography and the complementary aid of sonography the correct diagnosis should be made with confidence avoiding the need for invasive procedures as angiography and retrograde pyelography.

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Remember when lung cancer was a man's disease. Because men had been smoking longer than women. But the women's smoking boom that started in the 1930's and 40's—is paying most cruel dividends today. Yet most people still think lung cancer is a man's disease. Tell your female patients the true story. That lung cancer is now an equal opportunity tragedy. That's what "you've come a long way, baby" is all about.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
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**BRIEF SUMMARY**  
**PRDCARDIA® CAPSULES**  
(nifedipine)

For Oral Use

**INDICATIONS AND USAGE:** I. **Vasospastic Angina: PRDCARDIA** (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PRDCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. **Chronic Stable Angina (Classical Effort-Associated Angina):** PRDCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PRDCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in those patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PRDCARDIA and beta blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

**CONTRAINDICATIONS:** Known hypersensitivity reaction to PRDCARDIA.

**WARNINGS: Excessive Hypotension:** Although in most patients, the hypotensive effect of PRDCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PRDCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PRDCARDIA and a beta blocker, but the possibility that it may occur with PRDCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out.

**Increased Angina:** Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PRDCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

**Beta Blocker Withdrawal:** Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PRDCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PRDCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PRDCARDIA.

**Congestive Heart Failure:** Rarely, patients, usually receiving a beta blocker, have developed heart failure after beginning PRDCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

**PRECAUTIONS: General: Hypotension:** Because PRDCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PRDCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See Warnings.)

**Peripheral edema:** Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PRDCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

**Drug Interactions:** Beta-adrenergic blocking agents: (See Indications and Warnings.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PRDCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PRDCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis: Administration of PRDCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PRDCARDIA to avoid possible over- or under-digitalization.

Carcinogenesis, mutagenesis, impairment of fertility: When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose.

Pregnancy: Category C. Please see full prescribing information with reference to teratogenicity in rats, embryotoxicity in rats, mice and rabbits, and abnormalities in monkeys.

**ADVERSE REACTIONS:** The most common adverse events include dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PRDCARDIA or concomitant antianginal medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, diarrhea, constipation, inflammation, joint stiffness, shakiness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, and sexual difficulties. Very rarely, introduction of PRDCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

**Laboratory Tests:** Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted, and a single incident of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PRDCARDIA therapy is uncertain. These laboratory abnormalities have rarely been associated with clinical symptoms. Cholestasis, possibly due to PRDCARDIA therapy, has been reported twice in the extensive world literature.

**HOW SUPPLIED:** Each orange, soft gelatin PRDCARDIA CAPSULE contains 10 mg of nifedipine. PRDCARDIA CAPSULES are supplied in bottles of 100 (NDC 0069-2600-66), 300 (NDC 0069-2600-72), and unit dose (10x10) (NDC 0069-2600-41). The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

More detailed professional information available on request.



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*for the varied faces of angina*

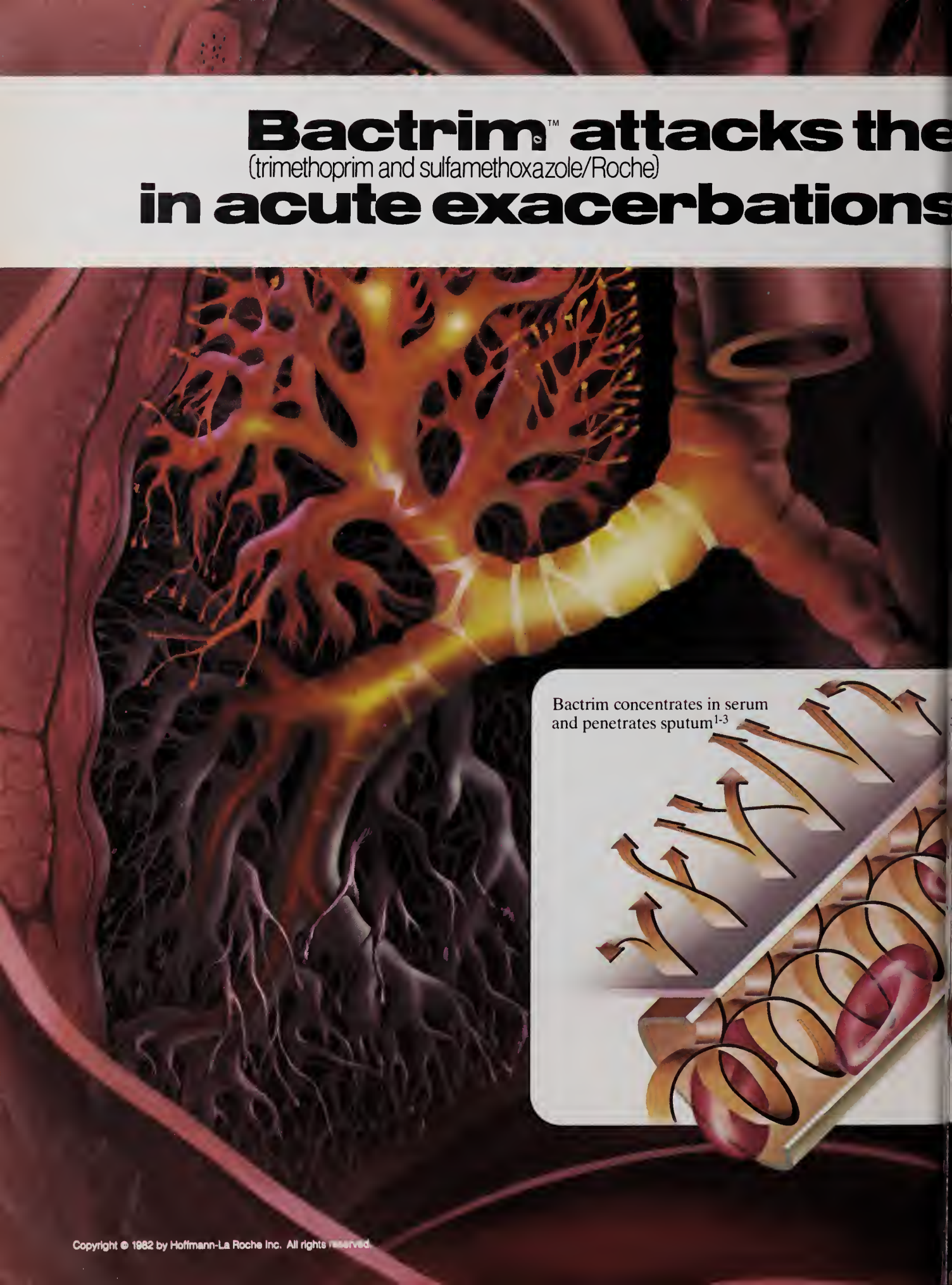
## **PROCARDIA<sup>®</sup>** **(NIFEDIPINE)** Capsules 10 mg

\*Procordia is indicated for the management of:

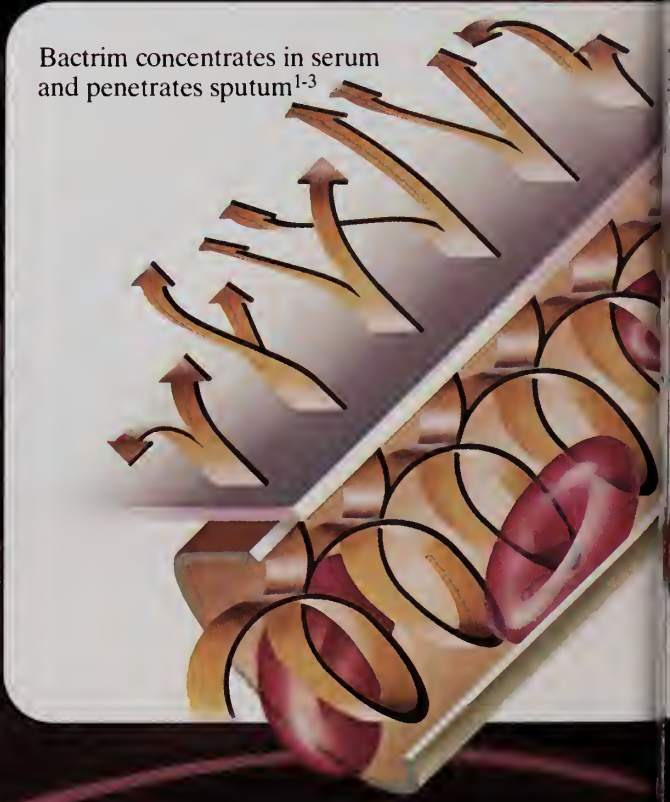
- 1) Confirmed vasospastic angina.
- 2) Angina where the clinical presentation suggests a possible vasospastic component.
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*Please see PROCARDIA brief summary on adjoining page.*

# **Bactrim<sup>™</sup> attacks the** (trimethoprim and sulfamethoxazole/Roche) **in acute exacerbations**



Bactrim concentrates in serum  
and penetrates sputum<sup>1-3</sup>





# major pathogens of chronic bronchitis\*

## Bactrim clears sputum of susceptible bacteria

In sputum cultures from patients with acute exacerbations of chronic bronchitis, *H. influenzae* and *S. pneumoniae* are isolated more often than any other pathogens.<sup>4,5</sup> One study of transtracheal aspirates from 76 patients with acute exacerbations found that 80% of the isolates were of these two pathogens.<sup>5</sup>

Bactrim is effective *in vitro* against most strains of both *S. pneumoniae* and *H. influenzae*—even ampicillin-resistant strains. And in acute exacerbations of chronic bronchitis involving these two pathogens, sputum cultures taken seven days after a two-week course of therapy showed that Bactrim eradicated these bacteria in 91% (50 of 55) of the patients treated.<sup>6</sup>

## Bactrim reduces coughing and sputum production

In three double-blind comparisons with ampicillin *q.i.d.*, Bactrim DS proved equally effective on all clinical parameters.<sup>7,9</sup> Bactrim reduced the frequency and severity of coughing, reduced the amount of sputum produced and cleared the sputum of purulence.

Bactrim has the added advantages of *b.i.d.* dosage convenience and a lower incidence of diarrhea than with ampicillin, and it is useful in patients allergic to penicillins.

Bactrim also proved more effective than tetracyclines in 10 clinical trials

involving nearly 700 patients.<sup>10</sup> Overall clinical condition of the patients, changes in sputum purulence, reduction in sputum volume and microbiological clearance of pathogens—all improved more with Bactrim therapy than with tetracyclines. G.I. side effects occurred in only 7% of patients treated with Bactrim compared with 12% of tetracycline-treated patients. (See Adverse Reactions in summary of product information on next page.)

Bactrim is contraindicated in pregnancy at term and nursing mothers, infants under two months of age, documented megaloblastic anemia due to folate deficiency and hypersensitivity.

Bactrim DS. For acute exacerbations of chronic bronchitis in adults\* when it offers an advantage over single-agent antibacterials.

**References:** 1. Hughes DTD, Bye A, Hodder P: *Adv Antimicrob Antineoplastic Chemother* 112:1105-1106, 1971. 2. Jordan GW et al: *Can Med Assoc J* 112:91S-95S, Jun 14, 1975. 3. Beck H, Pechere JC: *Prog Antimicrob Anticancer Chemother* 1:663-667, 1969. 4. Quintiliani R: Microbiological and therapeutic considerations in exacerbations of chronic bronchitis, in *Chronic Bronchitis and Its Acute Exacerbations: Current Diagnostic and Therapeutic Concepts*; Princeton Junction, NJ, Communications Media for Education, Inc., 1980, pp. 9-12. 5. Schreiner A et al: *Infection* 6(2):54-56, 1978. 6. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 7. Chodosh S: Treatment of acute exacerbations of chronic bronchitis: results of a double-blind crossover clinical trial, in *Chronic Bronchitis and Its Acute Exacerbations: Current Diagnostic and Therapeutic Concepts*. *Op. cit.*, pp. 15-16. 8. Chervinsky P: Double-blind clinical comparisons between trimethoprim-sulfamethoxazole (Bactrim™) and ampicillin in the treatment of bronchitic exacerbations. *Ibid.*, pp. 17-18. 9. Dulfano MJ: Trimethoprim-sulfamethoxazole vs. ampicillin in the treatment of exacerbations of chronic bronchitis. *Ibid.*, pp. 19-20. 10. Medici TC: Trimethoprim-sulfamethoxazole (Bactrim™) in treating acute exacerbations of chronic bronchitis: summary of European clinical experience. *Ibid.*, pp. 13-14.

attacks *H. influenzae*—even  
ampicillin-resistant strains



attacks *S. pneumoniae*



## Economical b.i.d.

# Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole/Roche)

\*Due to susceptible organisms. Please see next page for summary of product information.

# Bactrim™

(trimethoprim and sulfamethoxazole/Roche)

Before prescribing, please consult complete product information, a summary of which follows:

**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. **Note:** The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections. For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.

For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.

For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

Also for the treatment of documented *Pneumocystis carinii* pneumonia.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term; nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age.

**Warnings: BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL**

**PHARYNGITIS.** Clinical studies show that patients with group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hemopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions: General.** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin; reassess coagulation time when administering Bactrim to these patients.

**Pregnancy.** Teratogenic Effects. Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folate acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea, pseudomembranous colitis and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage: Not recommended for infants less than two months of age.**

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN**

**Adults:** Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

**Children:** Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

**For patients with renal impairment:** Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

**ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS**

**Usual adult dosage:** 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp (20 ml) b.i.d. for 14 days.

**PNEUMOCYSTIS CARINII PNEUMONITIS**

**Recommended dosage:** 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100, Tel-E-Dose® packages of 100, Prescription Paks of 20 and 28. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500, Tel-E-Dose® packages of 100, Prescription Paks of 40. Pediatric Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); cherry flavored—bottles of 100 ml and 16 oz (1 pint). Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); fruit-licorice flavored—bottles of 16 oz (1 pint).



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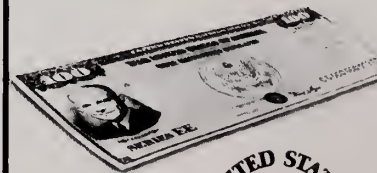
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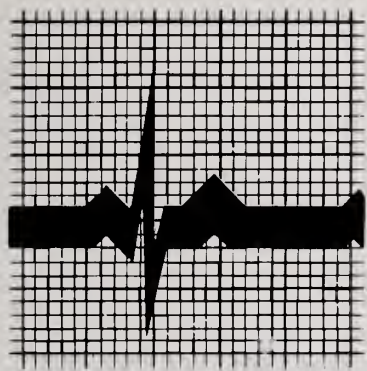


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# ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD, FACC

This 19-year-old male demonstrated dyspnea on exertion, easy fatigability, phocomelia, macrocephalus, bilateral pingueculae, an imperforate anus corrected surgically, clubbing, cataract, cyanosis since birth, multiple congenital anomalies, right ventricular enlargement (RVE), a loud, harsh systolic murmur and thrill at the left sternal border and below the left clavicle, and Hb of 18 g and Hct of 62%. Squatting

was noted. However, subsequently he was asymptomatic and did good work in high school. Chest roentgenograms showed thoracic scoliosis, hypoplasia of the left lung with loss of volume and opacity of the left hemithorax, shift of the heart and mediastinum to the left and increased vascularity of the right lung. The left pulmonary artery (LPA) was believed to be absent. See Figures 1 - 3.

Figure 1

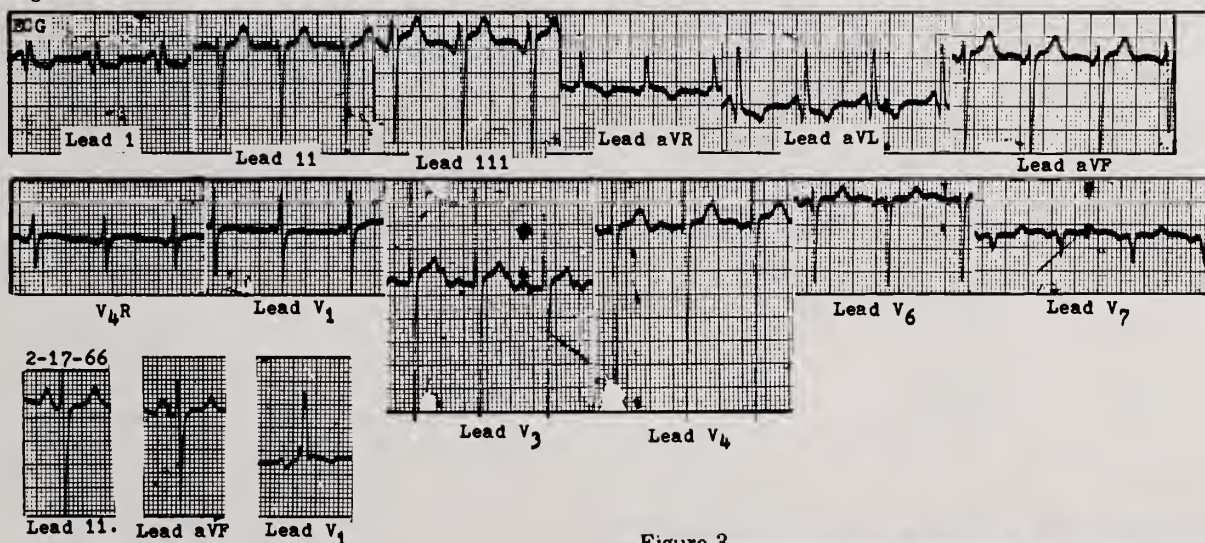
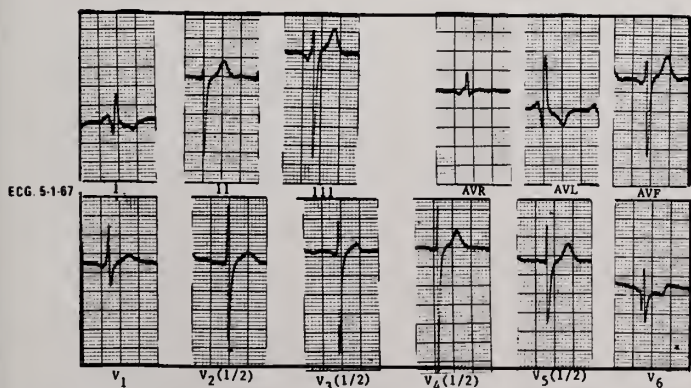
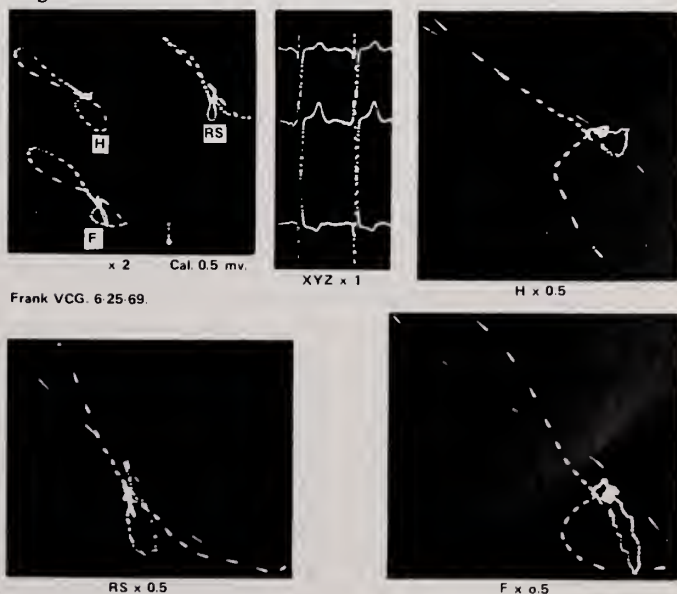


Figure 2



University of Puerto Rico, School of Medicine, Section of Cardiology,  
Rio Piedras, P.R. 00936.

Figure 3



## Questions

1. What are the electro-vectorcardiographic diagnoses?
2. What are the clinical diagnoses?

## Answers

Tetralogy of Fallot (TF). Post right Blalock-Taussig shunt in 10-17-66. Partial anomalous venous connection to the right atrium. Possible single ventricle.

Electrocardiograms (ECG) demonstrated RVE, left atrial enlargement, type IV left anterior hemiblock (LAH), left ventricular hypertrophy (LVH) and incomplete right bundle branch block.

The QRS axis= $-75^\circ$ . The P-R interval=0.12 sec., but only 0.09 sec. in some leads. The P waves and vectors were ill-defined, and of variable contours: a) rightward, posterior and superior, b) left superior, and c) inferior on 2-17-66. Deep S waves were present in leads II, III and aVF. Large biphasic complexes exist in  $V_2$ ,  $V_4$  (Katz-Wachtel phenomenon): q/Q waves in leads I, aVL,  $V_4$ -7 (or QS). ST-T wave abnormalities.

The vectocardiogram (VCG) demonstrated a figure-of-8 loop in the left anterior and right posterior quadrants, mainly superior. There is slight afferent loop slowing. The T loop is inferior and leftward, and the P loop is counterclockwise (CCW), left and superior.

## Comments

Anomalies of the pulmonary artery and its branches tend to occur in TF, this consistently being the LPA. When the LPA is absent there is a great tendency for the aortic arch to be right-sided (the opposite side). The murmur of pulmonic stenosis is stated to consistently radiate to the right upper chest.

The patient may belong to the *Vacterl* syndrome, and might be related to thalidomide ingestion by the mother, although the pregnancy and delivery were stated to be uneventful.

Left axis deviation, LAH and LVH, as in this patient, is certainly unexpected in classical TF. In the study of Feldt et al, 6.4% of 78 autopsied cases of TF were associated with preoperative vectocardiographic patterns similar to those of atrioventricular (AV) canal (which actually can coexist), that is, a CCW, superior leftward frontal loop. In these cases the distance between the AV node and the origin of left bundle branching was shorter and the fibers destined to become the right bundle branch took an elongated course, so that relatively early conduction to the left bundle branch system could transpire.

In the differential diagnosis several conditions must be considered: 1) Pentalogy or Trilogy of Fallot. In Pentalogy there may be increased magnitude of the initial septal vector secondary to right-to-left shunting at the atrial level reflecting

left ventricular overload; 2) Postoperative Blalock-Taussig shunt in TF— but this patient's ECG was similar to those illustrated prior to his shunt surgery. The Katz-Wachtel phenomenon may be present in one-third of postoperative TF ECGs; 3) TF can produce a posterior right QRS loop of RVH (type 1), somewhat similar to the VCG of this case; 4) Coronary sinus rhythm (high junctional) versus left atrial ectopic rhythm; 5) Short P-R interval. The P-R interval is usually normal in TF. However, sporadic cases of short P-R interval with a Wolff-Parkinson-White ECG have been documented in cases of tetralogy and pentalogy of Fallot.

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# Presentación de Casos

## Inferior Myocardial Infarction Concealed by a Complete Left Bundle Branch Block

Pablo I. Altieri, M.D.  
Héctor Banchs, M.D.  
José Martínez, M.D.

**Summary:** A patient with a documented inferior myocardial infarction developed a left bundle branch block and loss of the electrocardiographic evidence of the inferior myocardial infarction.

It is a well known phenomenon of the concealing of a inferior or anterior myocardial infarction by a left anterior hemiblock.<sup>1,2</sup> It is more rare the event of masking of an infarct by a complete left bundle branch block. It is the purpose of this report to describe a case of a left bundle branch block masking an old inferior myocardial infarction.

### Case Report

The patient is a 44 year old male patient who had a documented inferior myocardial infarction in 1980 (Fig. 1). Since then he has been followed at the cardiology clinic. On 11-3-81 he complained of chest pain and palpitations. An electrocardiogram at that time showed a complete left bundle branch block and absence of Q waves in leads II, III and AVF. This was interpreted as masking of the evidence of an old inferior myocardial infarction by the left bundle branch block. (Fig. 2)

Department of Medicine, Medical Science Campus, University of Puerto Rico.

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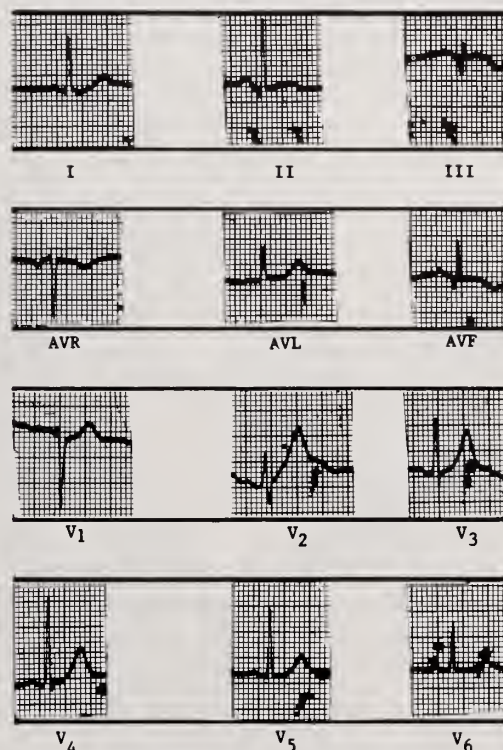


Fig. 1. Electrocardiogram showing Q waves in Lead III and AVF, compatible with an old inferior myocardial infarction.

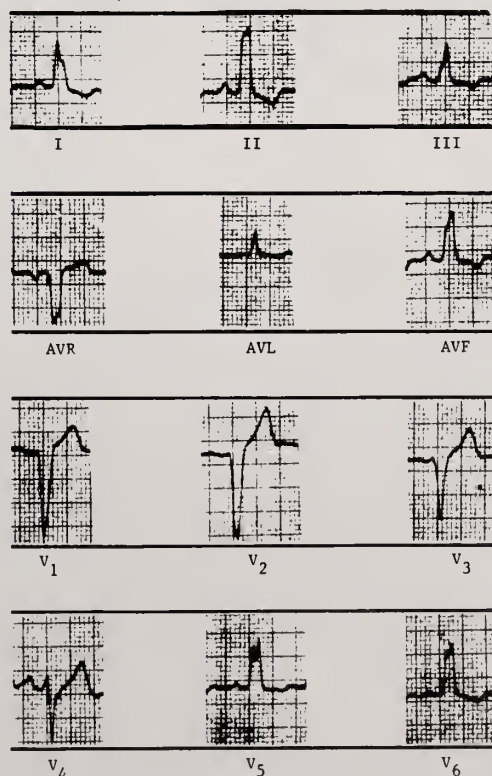


Fig. 2. Electrocardiogram showing a complete left bundle branch block with the disappearance of the Q waves and the evidence of the old inferior myocardial infarction.

## Discussion

Rosenbaum<sup>1</sup> and co-workers described intermittent left anterior hemiblock obliterating the findings of inferior wall myocardial infarction. This was explained on basis of initial forces directed inferiorly due to unopposed conduction over the left infero posterior fascicle of the left bundle.

In the frontal plane the initial forces in an inferior myocardial infarction are directed superiorly producing Q waves in the inferior leads.<sup>3</sup> In left bundle branch block the initial forces is directed to the left and usually inferior. The consistent leftward displacement of the initial deflection correlates well with the absence of the Q waves in lead I of the scalar electrocardiogram. Its inferior orientation is seen as an R wave in the inferior leads.

The development of a left bundle branch block in this patient and the recording of this initial inferior forces produced the masking of the Q waves in the inferior leads and the obscuring of the electrocardiographic manifestations of an inferior myocardial infarction.

In summary a patient is presented who lost all evidence of a previous inferior myocardial infarction with the development of a complete left bundle branch block. The recognition of the electrocardiographic abnormality is most difficult unless the phenomenon is intermittent or transient.

**Resumen:** Un paciente con un infarto inferior desarrolló un bloqueo completo de la rama izquierda produciendo la desaparición de la evidencia electrocardiográfica del infarto inferior.

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# RESUMENES PRIMER CONGRESO PUERTORRIQUEÑO DE CARDIOLOGIA



01

## MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION (AMI) IN THE CCU WITH THE USE OF INTRACORONARY STREPTOKINASE (IC-SK).

Pablo A. Guzmán, MD, FACC, Jeffrey A. Brinker, MD, The Johns Hopkins Hospital, Baltimore, Md.

IC-SK has been shown to be an effective form of treatment of thrombolysis in AMI. Limiting factors in the use of this therapeutic modality include availability of cardiac catheterization facility and experienced personnel. Since clot lysis and myocardial salvage are time dependent, successful application requires rapid mobilization and early application. We report the results of 3 pts. with AMI presenting to our CCU within 3 hrs. of onset of symptoms. Coronary angiograms (CA) were performed in CCU using routine Judkins approach. Image intensification was achieved by using a portable image intensifier (PII) (GE-polarix 2) and was recorded on an Eigen video disk recorder. This system with the assistance of a DUNN multi-image camera allows for obtaining hard copies of selected single frames of the CA. Adequate visualization of the occluded vessel was obtained in all. Two pts. had complete lysis of their obstructing thrombus with resolution of chest pain and ECG changes. The other patient had partial clot lysis. One patient upon lysis had recurrent life threatening ventricular arrhythmias which were easily recognized and treated in the CCU setting. Thus adequate CA can be obtained using a PII in the CCU with the aid of only routine nursing personnel, facilitating the prompt initiation of IC-SK. The CCU setting provides optimal facilities for treatment of complications associated with AMI and IC-SK.

02

## LOCALIZATION OF OLD MYOCARDIAL INFARCTION: ECHO-ECG CORRELATION. Rivera JR, Hernández E, Cintrón G, Linares E, Aranda JM. VA Hospital/U.P.R. School of Medicine, San Juan, Puerto Rico.

**Purpose:** To correlate the localization of pathologic ECG Q waves ( $>.03$  sec) with echocardiographic segmental contraction abnormalities (SCA) in patients (pts) with single old MI. Twenty three male pts ages 36 to 84 (mean = 61) with history and ECG evidence of single MI were compared with 11 normal males. Short axis views at the mitral valve (MV) and papillary muscle (PM) levels were analyzed. Each view was divided in octants, percent area shortening (%AS) of each octant was calculated and compared with a mean %AS of each corresponding octant in normals. A floating and a fixed axis systems were compared. ECG were categorized by a modification of the Minnesota code.

**Results:** All pts with inferior MI (IMI) had at least 1 SCA in the posterior wall by the fixed axis system but not by the

floating system (100% vs 80%). All pts with anterior MI (AMI) had at least 1 SCA in the anterior wall by either method. Examination at the MV level yielded the greatest number of SCA for both IMI and AMI (fixed system 100% in IMI and AMI, floating system 80% in IMI and 100% in AMI). Both systems yielded a high incidence of SCA in the contralateral wall in both IMI and AMI. **Conclusions:** Bidimensional echocardiography is a very sensitive mean of identifying SCA in pts with old MI. A fixed axis system appears to have the greatest yield. The high incidence of SCA in the contralateral segments warrants further evaluation.

03

## ISCHEMIC HEART RUPTURE. J.M. Suárez, J.M. Igartúa, G. Cintrón, J.M. Aranda, E. Hernández, G. Blanco, E. Linares. Veterans Administration Hospital and University of P. R. School of Medicine, San Juan, P.R.

**Purpose:** To review our clinical experience in patients (pts) with documented cardiac rupture (CR) secondary to acute myocardial infarction (MI). The records of all pts with proven MI complicated by CR from 1974-82 were studied. CR was documented at the operating room or at necropsy. Of 948 MI admissions, CR was identified in 19 pts (2%) and accounted for 18% (16/88) of all MI deaths. Eight pts (42%) had diabetes mellitus, eight (42%) had arterial hypertension and four (21%) had previous MI. Ten pts had left ventricular free wall rupture, all died, nine (90%) within 24 hours of admission, usually undiagnosed. Ventricular septal rupture was documented on an average of 3 days post MI on 8 pts, seven were operated and three survived. Fatal papillary muscle rupture was found in only one patient and was unsuspected. Anterior wall MI was present 7/10 (70%) of free wall ruptures and 4/8 (50%) of septal ruptures. **Conclusions:** 1) Of all MI deaths, at least 18% are related to CR. 2) Approximately 1/2 of all pts with CR had diabetes or hypertension and 21% had prior MI. 3) Free wall rupture usually occurs very early, frequently in pts with anterior MI, is unsuspected, undiagnosed and lethal. 4) Septal rupture occurs later, is usually diagnosed, may be repaired surgically with moderate success.

04

## "STREP AND STRETCH": DEFINITIVE THERAPY FOR CORONARY THROMBOSIS. Pablo A. Guzmán, MD, FACC, Jeffrey A. Brinker, MD, The Johns Hopkins Hospital Baltimore, Md.

The ability of intracoronary Streptokinase therapy (IC-SK) to lyse thrombi associated with acute myocardial infarction (AMI) has been well documented. However, residual coronary artery disease (CAD) can lead to early recurrence of symptoms and infarction. From a group of 9 pts. presenting within 5 hours of AMI and receiving IC-SK, 6 pts.



(66%) had successful thrombolysis. Of these 6 pts., one had normal coronary arteries and the remaining five had significant ( $>70\%$ ) CAD at the site of thrombosis. Of these, 2 had early symptomatic reocclusion of the affected vessel; one, who received only medical treatment has been asymptomatic at 6 months follow up; and 2 had successful immediate percutaneous coronary angioplasty (PCA) and are asymptomatic at 3 months on aspirin therapy only. In addition 1 pt. ten days post-MI who was intra-aortic balloon dependent because of post-MI angina underwent successful thrombolysis and immediate PCA of his single vessel LAD lesion. He remains asymptomatic also on aspirin therapy only.

Thus PCA appears to offer a safe and effective means of extending the benefits achieved by intracoronary thrombolysis and should be considered in all cases in which this procedure seems possible.

05

**LOW STRESS DENTAL PROCEDURES IN PATIENTS WITH RECENT ACUTE MYOCARDIAL INFARCTION.** AM Reyes, G Cintrón, R Medina, D Malaret, E Linares, JM Aranda, E Hernández, Veterans Hospital and University of P.R. School of Medicine, San Juan, Puerto Rico.

**Purpose:** To determine the safety of performing low stress dental procedures in patients (pts) within two weeks of acute myocardial infarction (MI). After informed consent, 15 pts participated in this study. Two Groups were identified; those not on beta blockers (Gr A, 11 pts) and those on beta blockers (Gr B, 4 pts). Lidocaine 2% with Epinephrine 1:100,000 was injected in the oral mucosa. Heart rate (HR), blood pressure (BP), electrocardiogram (EKG) and symptoms were monitored and recorded before, during and after the injection. Holter monitoring was performed 30 min. before to 3 hours after the procedure. Twelve lead EKG was obtained before and after the Holter and the day after.

**Results:** Gr A - Age 61 mean (51-71)  
Gr B - Age 58 mean (51-68)

Group	MI Days	Base Line	Dental Chair	Injection	5 min.	10 min.
A	12 (6-14)	BP HR <u>108</u> 73 70	BP HR <u>112</u> 73 71	BP HR <u>115</u> 74 70	BP HR <u>109</u> 72 67	BP HR <u>109</u> 73 67
B	12 (9-14)	BP HR <u>109</u> 68 75	BP HR <u>106</u> 71 76	BP HR <u>107</u> 71 67	BP HR <u>101</u> 68 68	BP HR <u>103</u> 69 66

None of the pts developed symptoms, MI, angina, hypotension, arrhythmias or EKG changes during or after the dental intervention. Low stress dental procedures are well tolerated by pts with recent ( $<2$  weeks) MI and can be safely performed.

**ELECTROCARDIOGRAPHIC AND SCINTIGRAPHIC CORRELATION OF ACUTE MYOCARDIAL INFARCTION:** O. Díaz, V. Toledo, J. Morales and F.M. Cortés.

Methods for reliably detecting, localizing and sizing acutely infarcted myocardium are desirable in order to select therapeutic damage. The purpose of this study is to demonstrate the sensitivity of PYP scan to detect and localize acute myocardial infarction as compared to the E.K.G.

We reviewed the records of 51 patients admitted to our institution with the suspected diagnosis of myocardial infarction in whom serial 12 lead ECG, cardiac isoenzymes profiles and PYP scanning were performed.

**Results:** Individual was as detected by:

Site	PYP	ECG
Anterior	13	8
Lateral	4	3
Apical	10	None
Inferior	14	7
Posterior	6	None
TOTAL	47	18

The incidence of false positive results by PYP scanning was 5.8% and only 1.9% by serial EKG. False negative results were observed in 7.8% by PYP scan and 31.3% by ECG.

In conclusion the ECG appears to be a less sensitive method, but more specific for detecting AMI. It also seems to be less sensitive in infarct localization.

**GATED CARDIAC BLOOD POOL STUDIES IN END STAGE RENAL DISEASE PATIENTS. J. V. Rivera, M.A. Ficek, O Larregoit, N. Quiñones, and A. Benitez. Veterans Administration Medical and Regional Office Center, San Juan, P.R.**

With the purpose of identifying patients with "uremic cardiomyopathy", cardiac blood pool studies (99m Tc-RBC) was performed in the following patient groups: end-stage renal disease without cardiac symptoms (ESRD-A), 8 patients; ESRD with cardiac symptoms (ESRD-S), 6 patients; myocardial infarction (MI), 20 patients; cardiomyopathy without renal disease or myocardial infarction (CM), 3 patients. Analysis included LVEF, RVEF, and wall motion studies in all and M-mode echocardiography in the renal patients.

Focal wall motion abnormality was found in 18/20 MI patients, and in 1/14 ESRD (A and S) patients. LVEF varied with the clinical status with a wide variation in the ESRD, CM, and MI groups.

This study suggests that absence of focal WM abnormalities may help differentiate patients with uremic cardiomyopathy from patients in whom coronary artery disease occurs in patients with ESRD.

08

**THE RELATIONSHIP BETWEEN RATINGS OF PERCEIVED EXERTION AND HEART RATE IN ACTIVE WHITE COLLAR PUERTORICAN MALES AGE 50 to 69 YEARS. M.A. Rivera and M.A. Albarrán, Dept. of Exercise Physiology, Sports Medicine Clinic, Condado, P.R.**

Evidence has not been found on the relationship between ratings of perceived exertion (RPE) and heart rate (HR) in S's over 50 years-old. In order to determine this relationship in a group of S's age 50 to 69 years, one hundred and twenty-two measures of RPE and HR were studied during graded exercise testing (GXT). GXT was administered to 15 S's ( $X \pm sd$ . Age (yrs)  $55.7 \pm 5.5$ , Height (cm)  $172.47 \pm 11.18$ , Weight (kg)  $81.81 \pm 14.68$ , % body fat  $18.40 \pm 3.71$ ,  $VO_2max$  (L/min)  $2.94 \pm 0.63$ ,  $VO_2max$  (ml kg min)  $37.03 \pm 8.72$ ). HR was recorded from the ECG using a Burdick EK6 electrocardiograph. The Spanish version of Borgs 15 point graded category scale was used to obtain RPE. Borgs validity data yielded  $r=0.85$  between RPE and HR for 30 to 50 years-old S's, (Lund Sweden. Glycerup: 1, 1962). Other investigators have reported r's between RPE and HR ranging from  $r = 0.42$  to  $0.94$ , (Med. Sci. Sports Exer. 14.390, 1982). HR and RPE were measured each minute during the GXT and were linearly related ( $r = 0.724$   $p < .001$ ),  $Y = 64.93 + 5.42(x)$ . These results indicate that for active white collar Puerto Rican males 50 to 69 years-old the spanish version of the Borg scale can be use as a clinical tool to monitor S's feelings of effort during GXT.

09

**SUPERVIVENCIA DE PACIENTES CON PRUEBA DE ESFUERZO MARCADAMENTE POSITIVA TRATADOS MEDICAMENTE. V. Arroyo, E. Linares, E. Hernández, G. Cintrón, J.M. Aranda, S. Cruz, V. Camacho. Hospital de Veteranos y Escuela de Medicina de la Universidad de Puerto Rico, San Juan, Puerto Rico.**

El propósito de este estudio fue determinar la supervivencia de pacientes (pts) con prueba de esfuerzo positiva con depresión del segmento ST 2 mm (P.E.+++ y tratados médicamente.

Se revisaron retrospectivamente las P.E.+++ y los expedientes clínicos de 90 pts así tratados durante los años 1973-82. La edad promedio fue de 56 años (varió de 40-69). El seguimiento promedio fue de 41 meses (varió de 1-108). Se usaron los protocolos de Bruce (76 pts) y de Naughton (14 pts.). **Resultados:** La supervivencia acumulada a 5 años fue de 90%. Nueve pts fallecieron durante el seguimiento, 7 de ellos de causa cardíaca. De acuerdo al trabajo cardíaco logrado durante la P.E.+++ , la supervivencia acumulada a 5 años fue como sigue:

Trabajo Cardíaco MET's (M)	Supervivencia a 5 años % SEM
9M (n=2)	100
7-9M (n=22)	94 $\pm$ 6
5-7M (n=39)	89 $\pm$ 5
5M (n=27)	86 $\pm$ 7

**Conclusiones:** 1) Todos los pacientes que alcanzaron 9M sobrevivieron y la supervivencia disminuyó al disminuir el trabajo cardíaco logrado en la P.E.+++ . 2) Pacientes con una P.E.+++ no tienen un pronóstico pobre.

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**PROFILE IN EJECTION FRACTION RESPONSE BY REST AND EXERCISE NUCLEAR VENTRICULOGRAPHY IN PATIENTS WHO UNDERWENT CORONARY BYPASS SURGERY. J.A. García-Gregory, M.D., F.A.C.C., A.S. Jackson, Ph.D., W.G. Squires, Ph.D., R. Gorten, M.D., Kelsey-Seybold Clinic, Houston, Texas.**

Exercise nuclear medicine procedures are widely used in the diagnosis and follow-up patients with coronary artery disease. To assess the changes in the profile of ejection fraction (EF) produced by coronary bypass surgery, the pre and post operative rest and exercise nuclear ventriculography (RNV) of 18 patients were examined. The patients ranging in age from 44 to 73 years were all symptomatic and had significant triple or quadruple vessel coronary disease. Complete revascularization surgery was performed at the Texas Heart Institute (Houston). None of the patients experienced intra or post operative complications. All patients had a (RNV) in the same lab at 8 weeks following surgery. A general improvement in wall motion in most bypassed areas was observed. All patients were asymptomatic after surgery. The pre and post operative EF's exhibited different ( $P < 0.01$ ) profiles at rest (RT), and exercise (EX), and recovery (RC). The pre op EF changes were linear. The means were: RT  $63.7 (\pm 19.7)$  EX  $67.0 (\pm 12.4)$ ; and RC  $70.9 (\pm 10.4)$ . The post op EF profile was non-linear, showing a more substantial rise with exercise (RT  $62.2 \pm 10.1$  and EX  $70.9 \pm 10.0$ ) with a slight decrease at RC ( $69.7 \pm 9.6$ ). The trend of increasing EF with exercise in post bypass patients have been reported before. We have noted that preoperative coronary disease patients showed a continued rise in EF during RC, while post op patients showed a decrease in the RC EF suggesting a decreased oxygen debt during exercise with earlier return to resting conditions.



# ACEBUTOLOL VERSUS PROPRANOLOL IN MODERATE TO MODERATELY SEVERE ESSENTIAL HYPERTENSION. Rivera A.L., Hernández, E. Veterans Administration Hospital and University of P.R. School of Medicine, San Juan, P.R.

The purpose of this study was to evaluate the safety and efficacy of the combination of a fixed dose of Hydrochlorothiazide (HCT 25 mg bid) and various doses of Acebutolol (A) compared to Propranolol (P) in the treatment of moderate to moderately severe essential hypertension (105-129 mm Hg sitting diastolic blood pressure DBP). **Results:** 33 pts (25 males and 8 females) whose mean age was 50 years (range 34-64) were randomized to P (18 pts) or A (15 pts). Both groups were similar in regard to age, cigarette smoking and alcohol use. The average baseline DBP in the P. group (mean  $\pm$  S.D. =  $116 \pm 5.2$  mm Hg) was significantly higher ( $p < .01$ ) than in the A group  $111 \pm 3.9$  mm Hg). Six (33%) of the 18 P group pts were dropped during the study (2 drug failures, 2 adverse effects, 2 unrelated illness). Of the 15 A group pts, 3 (20%) were dropped (1 drug failure, 1 adverse effect, 1 unrelated illness). These differences were not statistically significant. No difference between both groups was found in the percentage of pts achieving or maintaining acceptable DBP or in the number of dropouts or adverse effects. The percentage of DBP drop with the combination of HCT and beta-blocker was similar in both groups (A=19.1%, P=20.4%). **Conclusions:** A combined with HCT is a new combination as effective as P in the treatment of moderate to moderately severe essential hypertension. The drug is safe and usually well tolerated.

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# INFLUENCE OF AGE & SEX ON EXERCISE BLOOD PRESSURES: A CROSS SECTION ANALYSIS OF A CLINIC COHORT. J.A. García-Gregory, M.D., A.S. Jackson, Ph.D., E.F. Beard, M.D., W.G. Squires, Ph.D. Kelsey-Seybold Clinic, Houston, Texas.

Data from epidemiological research show age and sex are related to resting blood pressure. This study examined the effects of aging and sex on exercise systolic blood pressure (ESBP). From a total cohort of 4,865 patients who received an exercise stress test at Kelsey-Seybold Clinic, 2,199 male (M) and 422 female (F) patients were found who had a normal exercise EKG and exceeded 90% of age predicted Max HR. The mean ages were  $43.9 (\pm 10)$  and  $44.8 (\pm 11.5)$  for M and F. The M had higher ( $P = 0.001$ ) BP at rest; SBP  $125 (\pm 16)$  vs  $121 (\pm 19)$  and DBP  $83 \pm 10$  vs  $79 \pm 11$ . The mean ESBP of M ( $182 \pm 25$ ) was higher ( $P < 0.001$ ) than F ESBP ( $160 \pm 25$ ). Multiple regression was used to assess the effects of RSBP, age and sex on ESBP. The terms RSBP, age and their interaction accounted for ESBP variance ( $P < 0.01$ ). Sex and the interaction of sex with the multivariate function of RSBP and age accounted for additional ESBP variance ( $P < 0.05$ ). A plot of M and F regression lines showed changes in ESBP over ages were not parallel; the slope of the F age-ESBP regression line was steeper than the M slope. We concluded that the effects of aging on ESBP are different for M and F and the trend is not due to the influence of aging on RSBP. These results demonstrate the need for different criteria when evaluating ESBP response of M and F.

# THE IMPORTANCE OF HEMODYNAMIC AND ECHOCARDIOGRAPHIC EVALUATION PRIOR TO THE INSERTION OF A PERMANENT PACEMAKER IN THE ELDERLY. Héctor Banchs, Pablo I. Altieri, José Martínez Toro, Efraim Defendini, Luis Piñeiro, Juan González. Department of Medicine and Surgery, University, of Puerto Rico, Medical Science Campus.

The modern pacemaker modality of Universal Pacing (D.D.D.) has been under investigation at our laboratory. Our approach has been to study these patients (P.), specially the elderly ( $> 60$  years) hemodynamically (direct arterial pressure) and echocardiographically. Six P. (Group I) with a mean age of 62 years have been studied. The baseline systolic blood pressure (S.B.P.) and with atrioventricular synchrony was  $116 \text{ mmHg} \pm 73$  which was reduced with ventricular pacing to  $86 \text{ mmHg} \pm 86$  ( $P < .005$ ). The P. developed dizziness during this lowering. The pacing rate with each modality was 72 beats/min. The echocardiograms of group I during pacing was compared with a control group which did not drop the S.B.P. during ventricular pacing (Group II). The ejection fraction (E.F.) of Group I by echocardiography was  $< 50\%$ . The E.F. of group II was  $> 50\%$  and increased during ventricular pacing. It was noticed an increase in systolic contractility of the septum during systole when A-V synchrony was maintained. No ventricular arrhythmias or ventricular atrial conduction were observed.

In conclusion when the decision to insert a pacemaker in the elderly ( $> 60$  years) is done, the hemodynamic status of the P. should be defined to avoid the pacemaker syndrome. In P with an E.F.  $< 50\%$  with reduction of the S.B.P. during ventricular pacing a D.D.D. or A.V., sequential pacemaker should be considered.

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# ECOCARDIOGRAFIA BIDIMENSIONAL EN TETRALOGIA DE FALLOT. Jorge Sánchez, M.D., José T. Medina, M.D. C-T Radiology Complex, Bayamón, P.R.

Con propósito de evaluar los componentes de la tetralogía y su evolución, se obtuvieron 16 ecos bidimensionales en 14 pacientes: 5 sin cirugía, 5 con Blalock-Taussig y 4 con cirugía correctiva, con edades de 2 meses a 14 años. Trece tienen cateterismo y angiografía. El defecto interventricular infundibular grande se evaluó en el eje paraesternal largo (EPL). Los 4 corregidos tienen un parche radioluciente, sin defecto residual. El tamaño aórtico y grado de cabalgamiento (20-70%) se vió en el EPL. Los grados de estenosis infundibular y valvular se evaluaron en el eje corto a nivel aórtico. La hipertrofia ventricular derecha se observó en EPL y de 4 cámaras. Las arterias pulmonares y el atrio izquierdo crecieron con Blalock-Taussig adecuado. El arco aórtico fue izquierdo y se visualizó junto con las arterias pulmonares en vistas supraesternales. Los pacientes corregidos presentaron movimiento paradójico del septo, estenosis residual, insuficiencia pulmonar y aneurismas del tracto de salida de ventriculo derecho.

Concluimos que el eco bidimensional permite evaluar adecuadamente en forma no invasiva, las variedades de tetralogía, los defectos asociados y los cambios producidos por cirugía paliativa y correctiva.

# INCIDENCIA DE CONDUCCION RETROGRADA (VENTRICULO-ATRIAL) EN NIÑOS Y ADOLESCENTES. J. Villafañe, M.D.; A.F. Espinosa-López, M.D.; A. Martínez-Picó, M.D. Hospital Pediátrico Universitario y RCM, UPR.

El grupo de estudio consiste de 12 pacientes de 3 a 18 años de edad los cuales fueron sometidos a estudios electrofisiológicos intracavitarios recientemente. Los diagnósticos clínicos incluían variados defectos de conducción y disritmias. Cuatro de los pacientes tenían cardiopatías congénitas, 3 de ellos habiendo sido sometidos a cirugía correctora previo al estudio. Se encontró disfunción del nódulo sinoatrial (8), cuatro de éstos asociados a disfunción del nódulo atrio-ventricular, ritmo Hisiano (1), bloqueo supra Hisiano completo (2), prematuros ventriculares (1).

Para determinar la presencia de conducción retrógrada a todos se les estimuló el ventrículo derecho utilizando un marcapasos externo programado a diferentes intervalos mientras se obtenía electrogramas intracavitarios en el ventrículo y atrio derecho. A la misma vez se obtuvo electrocardiograma de superficie y trazado de presión arterial. Se comprobó la presencia de conducción retrógrada en cinco pacientes al obtener trazados con deflecciones ventriculares seguidas por deflecciones atriales a intervalos constantes durante la estimulación. Nuestra incidencia de conducción retrógrada de 41.7% aparenta ser menor que las informadas por otros grupos.

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# EFUSION PERICARDICA LUEGO DE IMPLANTACION DE MARCAPASOS BICAMERALES CON CABLES CONDUCTORES EPICARDICOS. J. Villafañe, M.D.; M. Vega-Vidal, M.D.; A.F. Espinosa-López, M.D.; E. Márquez, M.D.; A. Martínez-Picó, M.D. Depto. de Pediatría y Cirugía, Hospital Pediátrico Universitario y Escuela de Medicina, U.P.R.

Se revisaron las historias clínicas de 11 pacientes de 7 a 19.5 años de edad con marcapasos permanentes y cables epicárdicos 5 de estimulación ventricular (VVI) y 7 bicamerales (MPB), implantados entre enero a sept. de 1982. Seis de los MPB fueron implantados en nuestra institución. Todos los pacientes con MPB y uno de los VVI desarrollaron efusión pericárdica leve (2) o moderada (6), de 4 a 13 días post implantación, confirmada por ecocardiogramas. Los pacientes con efusión moderada recibieron corticoesteroides por vía oral por un promedio de 32 días. La estadía en el hospital fue de 18 a 57 días. No hubo mortalidad asociada a esta complicación. En 37 pacientes con VVI y cables epicárdicos ventriculares implantados entre el 1960 a 1981 en nuestra institución la incidencia de efusión pericárdica fue de 8%. Esto contrasta con la alta incidencia en los pacientes con MPB en los cuales se utilizó un cable conductor atrial en adición al ventricular. Esta complicación, la morbilidad asociada a su tratamiento y además, el tiempo de estadía en el hospital puede disminuirse con el uso de cables endocárdicos.

# EFFECT OF SUBINHIBITORY CONCENTRATIONS OF ANTIBIOTICS ON THE ADHERENCE OF *S. AUREUS* AND *ENTEROCOCCUS* TO HEART VALVES. C.H. Ramírez-Ronda, MD, Depts. of Medicine and Research, VA Medical Center and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

Antibiotics are frequently used in the prophylaxis of bacterial endocarditis, two frequent pathogens are *S. aureus* and *Enterococcus*; the prophylactic regime utilizes a penicillin, a penicillin plus an aminoglycoside, erythromycin or vancomycin. Since many times the concentrations in serum are inappropriate because of dose timing and/or absorption. We studied the effects of exposure and growth of bacteria in subinhibitory concentrations of penicillin, ampicillin, vancomycin, gentamicin and erythromycin on their adherence to heart valves covered with fibrin and platelets. For *Enterococcus*, adherence was decreased from 5400 to 1290 by penicillin, to 1360 by ampicillin, to 750 by vancomycin, to 5200 by gentamicin and to 1403 by erythromycin. For *S. aureus*, adherence decreased from 2900 to 690 by penicillin, to 710 by ampicillin, to 400 by vancomycin, to 2801 by gentamicin and to 723 by erythromycin. The antibiotics utilized were effective in decreasing adherence for all strains except gentamicin which is known to be unable to penetrate the cell wall easily. This effect may help explain the effectiveness of these agents in the prophylaxis of endocarditis.

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# URGENT CARDIAC VALVE REPLACEMENT DUE TO INFECTIVE BACTERIAL ENDOCARDITIS, JM Igartúa, G Cintrón, E. Hernández, E Linares, G. Blanco, JM Aranda. VA Hospital, University of P.R. School of Medicine, San Juan, Puerto Rico.

**Purpose:** To assess the clinical characteristics, outcome and medical care costs of patients (pts) submitted to urgent cardiac valve replacement (CVR) due to infective bacterial endocarditis (IBE). **Methods:** Retrospective review of all pts needing urgent CVR due to IBE between 1977-81. **Results:** 12 pts fulfilled the study criteria, mean age 48 years (38-64). Nine did not have predisposing cardiovascular diseases or interventions. Mean duration of symptoms was 4 weeks, and 4 pts received prior antibiotics. All pts had severe heart failure as the indication for CVR, mainly due to aortic regurgitation. Blood cultures were positive in 8 pts, 7 for streptococci. Echocardiography was positive in 11 pts; vegetations or mitral valve fluttering was seen in 10. Eight pts underwent single CVR, 2 double and 2 single plus repair of ruptured interventricular septum. Four pts died, 2 at surgery, 2 in the postoperative period. All but 1 of the survivors had major postoperative complications. Mean duration of hospitalization was 8 weeks and average cost was \$15,060/pt, 2 1/2 times the cost of elective heart surgery. **Conclusions:** In this study, pts with IBE needing urgent CVR usually had no identifiable predisposing factors; streptococcal aortic valve involvement with severe heart failure predominates; early echocardiography was usually positive, surgery and antibiotic therapy was life-saving in 2/3 of pts although the post-operative course was complicated, prolonged and expensive.



**CARDIOVASCULAR CRITICAL CARE UNIT EXPERIENCE IN POST-OPERATIVE 312 PATIENTS.** Iván J. Lladó, MD., Migdalia I. González, MD., Elsa Robledo, RN., Efraín Defendini, MD., Enrique Márquez, MD., Nydia R. De Jesús, MD., Gumersindo Blanco, MD., Rafael Brito, MD.

A 14 months experience of 312 patients (pts.) were reviewed for morbidity; mortality incidence and cost effectiveness of services render.

**Study Group Characteristics and Mortality: (30 days)**

TN: 312	NO.	CHD	AHD	ECSD	% M
Adults (22-84 y/o $\bar{44}$ )	138 (45%)	8	109	21	7%
Pediatrics (1 day-21 y/o $\bar{7}$ )	174 (55%)	86	24	64	6.8%

CHD: Congenital Heart Disease; AHD: Acquired; ECSD: Emergency Cardio Surgical Disease; % M: % Mortality

**Morbidity Incidence by Systems:**

TN Complications: 803

Systems	DX Lab.	N.	n/N %
Cardiovascular	EKG.	385	48%
Hematologic	CBC, PT, Hcto PTT	265	33%
Respiratories	ABG, X rays	88	11%
Infectious	Microbiology	32	4%
Others	U/A, SMA-18	33	4%

**Conclusions:**

- (1) The CICU mortality incidence over 48 hrs. post-operatively happened on ECSD and IV vessel Emergent Aorto Coronary By Pass; in 7 of 312 pts. for 2.2% M.
- (2) Cardiovascular and Hematologic systems were mostly affected immediately post-op.
- (3) CBC, PT, PTT, SMA-18 and U/A had no conclusive DX value as standard laboratory orders.

**SUBXYPHOID APPROACH IN THE IMPLANTATION OF DUAL CHAMBER PACEMAKERS.** Héctor Banchs, Pablo I. Altieri, Efraín Defendini, Romulo Suero, José Martínez Toro. Department of Medicine, University of Puerto Rico. Medical Science Campus.

The implantation of dual chamber pacemakers usually is done by the intravenous route. We have inserted 15 Universal pacemaker (D.D.D.) Medtronic Model 7000 or 7000A via the subxyphoid approach with minimal complications. There were 6 patients (P.) with sick sinus syndrome and 9 with atrio-ventricular block. All P. had previous electrophysiological and hemodynamic studies including arterial blood pressure and echocardiography during A-V synchrony and ventricular pacing. It was noticed that during ventricular pacing alone in the elderly (age > 60 year), there was a statistically significant systolic blood pressure drop from 116mmHg to 80mmHg ( $P < .005$ ). Arterial blood pressure alternans was observed in 4 P. during ventricular pacing. The ejection fraction (E.F.) of this group was less than 50%. The E.F. of the nonhypotensive group was > 50%. Importance was given during the electrophysiologic study and at implantation to ventricular atrial conduction and the A-V interval. No ventricular arrhythmias or competitive rhythms were found in the longitudinal follow up. Only 2 P. developed a pleuropericardial reaction which resolved with medications.

In conclusion the dual chamber pacemakers in the elderly is useful because it maintains the A-V synchrony. The hypotension usually is seen in P. with a reduced E.F. and a stiff left ventricle. The implantation can be done without big complications via the subxyphoid approach. A movie will be shown to explain the technique.

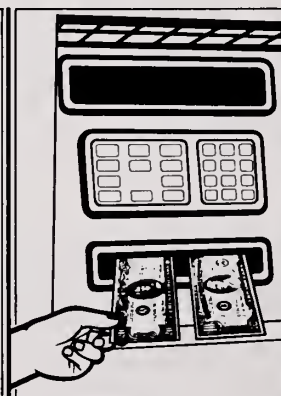
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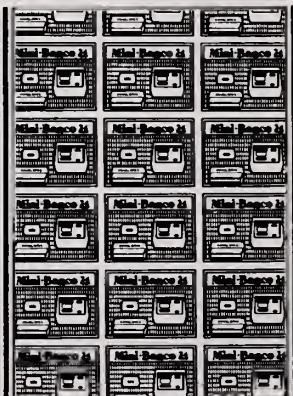
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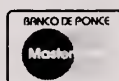
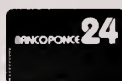
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# RESUMENES XXV CONFERENCIA MUNDIAL DE LA UNION INTERNACIONAL CONTRA LA TUBERCULOSIS BUENOS AIRES

**E**n Buenos Aires, Argentina durante los días 11 al 15 de diciembre de 1982 se celebró la XXV Conferencia Mundial de la Unión Internacional Contra la Tuberculosis. He querido compartir con ustedes los resúmenes de los trabajos más sobresalientes sobre la quimioterapia antituberculosa allí presentados.

Es bien significativo el hecho que el problema de la tuberculosis, aunque siempre presente en todas las sociedades del urbe, se ha ido controlando grandemente. Pero se está observando que las sociedades más avanzadas, y que creían tener este problema resuelto, están siendo obligadas por sus experiencias en los últimos años a no descuidarlo y a dedicarle los recursos que a este problema le habían quitado al creerlo resuelto.

**Ramón Figueroa Lebrón, M.D., F.C.C.P.**  
Presidente, Sección de Neumología  
Asociación Médica de Puerto Rico

## QUIMIOTERAPIA DE LA TUBERCULOSIS

**TRATAMIENTO DE CORTA DURACIÓN DE LA TUBERCULOSIS PULMONAR CON RIFAMPIN - ISONIACIDA DOS VECES POR SEMANA (EN SU MAYOR PARTE) EN UN PROGRAMA DE TRATAMIENTO EN EL TERRENO: CINCO AÑOS DE EXPERIENCIA.**

*A.K. Dutta\*, D. Moers y W.W. Stead*

En muchos ensayos clínicos controlados, se ha podido comprobar la eficacia de diversos esquemas de quimioterapia de corta duración para la tuberculosis pulmonar. Existe poca información sobre los resultados de esta terapia en los programas de tratamiento en el terreno. Desde enero de 1976 hemos tratado 760 pacientes con tuberculosis pulmonar bacteriológicamente comprobada, según un esquema que utiliza 600 mg de rifampin (RIF) y 300 mg de isoniácida (INH) diariamente durante un mes, seguido de 600 mg de RIF y 900 mg de INH dos veces por semana durante otros ocho meses. El tratamiento es administrado y supervisado por 45 médicos y enfermeras de Salud Pública en 70 dispensarios locales de enfermedades respiratorias del Programa contra la Tuberculosis de Arkansas. La negativización bacteriológica del esputo se produjo dentro de los dos primeros meses de tratamiento en el 67% de los casos y dentro de los

tres primeros meses en 90%. Los efectos secundarios importantes fueron: la hepatitis (3,8%) y las reacciones de hipersensibilidad como el "síndrome gripal" y la trombocitopenia (sólo 1%). El tratamiento fracasó durante la terapia en 1,2% y las muertes debidas a la tuberculosis ocurrieron en el 1% de los casos. Quinientos cincuenta y cuatro (554) pacientes que completaron el tratamiento fueron seguidos durante seis a 58 meses; de éstos, 7 (1,3%) presentaron recaídas, todos, salvo uno, dentro de los seis meses después de la suspensión del tratamiento y con bacilos sensibles a ambas drogas. Así se registró un éxito total en 96.5% de los pacientes que completaron el tratamiento. Esta terapia es exitosa en los tratamientos de terreno y presenta las ventajas de facilitar la supervisión de la administración, cuando esté indicado, y de tener un costo bajo.

\* Veterans Administration Medical Center, 300 E. Roosevelt, Little Rock, AR 72206, Estados Unidos.

**TRATAMIENTO DE LA TUBERCULOSIS PULMONAR CON UN ESQUEMA AUTOADMINISTRADO DIARIAMENTE, DURANTE SEIS MESES, QUE CONTIENE ISONIACIDA Y RIFAMPICINA: INFORME DE UN ESTUDIO CLINICO COOPERATIVO DEL SERVICIO DE SALUD PUBLICA DE LOS ESTADOS UNIDOS.**

*D.E. Snider Jr.\*, M. Long y L.S. Farer*

Esta experiencia terapéutica en doble ciego efectuada en los Estados Unidos compara la eficacia de dos esquemas de tratamiento autoadministrados diariamente, uno de seis meses y el otro de 15 meses. Durante los seis primeros meses todos los pacientes recibieron 300 mg de isoniácida y 600 mg de rifampicina todos los días. Durante los siguientes nueve meses de tratamiento, los enfermos asignados al grupo de 15 meses recibieron 300 mg de isoniácida y etambutol 15 mg/kg, diariamente, mientras que los asignados al grupo de seis meses recibieron un placebo. Se incluyó un total de 672 enfermos que provenían de 15 centros de tratamiento, que cumplían con las condiciones requeridas. Treinta y cinco (35) enfermos (5.2%) presentaron reacciones secundarias a la isoniácida, a la rifampicina o a ambas. Veintiuno (21) tuvieron reacciones tóxicas hepáticas y 14 otro tipo de reacciones adversas. De los 379 pacientes que completaron el tratamiento inicial de cuatro meses, 187 fueron asignados al esquema de seis meses, y 192 al de 15 meses. Durante los 18 meses de observación después del tratamiento, la proporción de recaídas fue significativamente más elevada en el grupo de enfermos del esquema de seis meses (9%) en comparación con el de 15 meses (0%).

\* Tuberculosis Control Division, Center for Prevention Services, Centers for Disease Control, Atlanta, Georgia 30333, Estados Unidos.

# COMPARACION DE TRES ESQUEMAS DE SEIS MESES PARA CASOS FROTIS POSITIVOS DE TUBERCULOSIS PULMONAR. UNA INVESTIGACION DE: SINGAPORE GOVERNMENT TUBERCULOSIS SERVICES Y BRITISH MEDICAL RESEARCH COUNCIL.

Coordinadores: S. Devi, T. Tiong-Har y T. Seng-Kee, Singapur y D. Girling, Reino Unido. E\*

Este estudio compara tres esquemas terapéuticos de seis meses, todos los cuales incluyen una fase inicial diaria de uno o dos meses, seguida de cuatro o cinco meses de tratamiento con isoniácida y rifampicina dada intermitentemente tres veces por semana. Los esquemas estudiados fueron: 2SHRZ/H3R3, ISHRZ/H3R3 y 2HRZ/H3R3 (S: estreptomicina, H: isoniácida, R: rifampicina y Z: pirazinamida). Se evaluó el rol de la estreptomicina en la fase inicial y los efectos de una reducción de la fase inicial de dos meses a uno. Entre abril de 1979 y noviembre de 1980 se admitieron en el estudio a un total de 303 pacientes con tuberculosis pulmonar positiva al examen directo. Se dispondrá de los últimos resultados del tratamiento y de los índices de recaídas de 85 pacientes por cada esquema con un seguimiento de seis meses después de finalizado el tratamiento y de 70 pacientes por cada esquema con un seguimiento de 12 meses después del tratamiento.

\* Ministry of Health, 9th Storey, Cuppage Center, 55 Cuppage Road, 0922 Singapur.

## ESTUDIO CLINICO DE LOS REGIMENES DE SEIS MESES QUE CONTIENEN PIRAZINAMIDA EN EL TRATAMIENTO DE LA TUBERCULOSIS PULMONAR. RESULTADOS PRELIMINARES.

P. Maasilta\*

En una población finlandeses que presentaban tuberculosis pulmonar bacilífera, se compararon dos regímenes de seis meses que contenían rifampicina (R) e isoniácida (H) diariamente, con pirazinamida (Z) administrada en la fase intensiva inicial, durante dos semanas en uno de los esquemas y durante seis semanas en el otro. El objetivo era estudiar la duración mínima necesaria de administración de Z y apreciar los efectos adversos sobre el hígado de esta asociación de medicamentos, potencialmente hepato-tóxica, en una población con alta frecuencia de alcoholismo. El estudio sigue en curso: 120 enfermos comenzaron la quimioterapia. La eficacia del tratamiento fue evaluada por la tasa de negativización de los cultivos a los dos meses y por la tasa de recaídas durante el primer año después de la suspensión del tratamiento. Los resultados preliminares indican que con los dos regímenes se obtuvo una negativización de los cultivos en más del 90% de los enfermos. Las reacciones adversas fueron leves y en cuatro pacientes fueron motivo de la modificación del tratamiento.

\* Department of Pulmonary Diseases, University Central Hospital, Helsinki, Haartmaninkatu 4, 00290 Helsinki 29, Finlandia.

## ESTUDIO PILOTO CON QUIMOTERAPIA DE CORTA DURACION (3 + 3 MESES), CON ESQUEMAS INICIALES CUADRUPLAS (HRSZ) E INTERMITENTES (2/7) PARA CASOS NUEVOS DE TUBERCULOSIS POSITIVOS AL EXAMEN DIRECTO.

C. Anastasatu\*, O. Bercea y E. Corlan

Un total de 720 nuevos casos de tuberculosis positivos al examen directo provenientes de 10 distritos de Rumania fueron distribuidos al azar a partir de 1980 en los siguientes esquemas: A. 3RHSZ<sub>2</sub>/3RH<sub>2</sub>; B. 3RHSZ<sub>2</sub> y C. 3RHE<sub>2</sub>/6HS<sub>2</sub>, a fin de evaluar la eficacia, en condiciones de rutina, de esquemas de seis meses de duración intermitentes desde el comienzo, seleccionados mediante un estudio previo, en comparación con el esquema estándar de nueve meses aplicado en nuestro país. A excepción de 16 casos (12 perdidos de vista y cuatro muertes), se evaluaron 704 pacientes (259, 250 y 195, respectivamente) al fin del tratamiento. Se modificó el régimen de 13 pacientes (1,8%) debido a resistencia anterior al tratamiento y el de 28 (3,9%) debido a efectos secundarios; 126 pacientes (17,5%) no cumplieron con el tratamiento. No se logró quiescencia bacteriológica en 15 casos únicamente (2,1%). Todos ellos (tres del esquema A, cinco del B y siete del C) pertenecían al grupo que no había cumplido el tratamiento.

De 260 casos con un mínimo de seis meses de seguimiento después del fin del tratamiento, 21 (8,1%) recayeron: tres (3,1%) del grupo A, cinco (5,2%) del grupo B y 13 (20%) del C. Las recaídas predominaron entre quienes no habían cumplido con el tratamiento.

\* Tuberculosis Research Institute, Sos. Viilor 90, sect. 4, 75239 Bucarest, Rumania.

## ENSAYO QUIMIOTERAPEUTICO CONTROLADO DE CUATRO ESQUEMAS DE SEIS MESES EN EL TRATAMIENTO DE LA TUBERCULOSIS PULMONAR.

H. Baba\*, A. Shinkai, R. Izuchi e Y. Azuma

Se compararon cuatro esquemas quimioterapéuticos administrados durante seis meses, seguidos de períodos de observación de 18 meses a cuatro años. A partir de octubre de 1975 y durante un período de tres años y tres meses, 520 casos consecutivos fueron repartidos al azar entre los cuatro esquemas siguientes: 3RHS/3RHS<sub>2</sub>, 2RHZS/4RHZ, 2RHZE/4RHZ, 2RHES/4RHE. Cada serie estaba compuesta de 130 sujetos. Las condiciones elegidas para la inclusión de los enfermos en este estudio eran: ser admitido en nuestro hospital, no haber sido tratado o haber sido tratado durante menos de 15 días, frotis positivos, edad de 15 años o más; la cavidad más grande no debía sobrepasar cinco centímetros de diámetro. Después de la exclusión de los casos que no cumplían con los requisitos, quedaron 445 casos para el análisis final. La expectoración fue examinada una vez por semana durante los tres primeros meses, y luego una vez al mes. A la 8a. semana, 73,3% de los casos se habían negativizado y al 5o. mes, 100%. No se constataron efectos secundarios graves. Hubo 25 recaídas bacteriológicas, 8%, 2,7%, 0,9% y 10,8% respectivamente, según los esquemas enumerados más arriba.



En conclusión, los esquemas que contenían pirazinamida se mostraron más eficaces. En el momento de la conferencia, se mostrarán resultados de un período de observación más largo.

\* National Nakano Chest Hospital, 20-14-3 Egota Nakano-Ku, Tokio 165, Japón.

## RESULTADOS DEFINITIVOS DE UN ESTUDIO TERAPEUTICO CONTROLADO QUE COMPARA CUATRO REGIMENES "PESADOS", DE QUIMIOTERAPIA DE CORTA DURACION DE LA TUBERCULOSIS PULMONAR.

*D. Larbaoui\*, Z. Lamrani y F. Boulahbal*

El objeto de este estudio terapéutico es la evaluación de cuatro regímenes cortos de seis meses, de aplicación posible a todos los casos de tuberculosis pulmonar, con cepa ya sea resistente o sensible. Cuatrocientos (400) enfermos con tuberculosis pulmonar bacteriológicamente confirmada, fueron sometidos, según una distribución al azar, a uno de los cuatro regímenes terapéuticos estudiados: R.I.: 24 RHZP 7/7; R.II.: 8 RHSP 7/7 + 16 RHP 2/7; R.III.: 8 RSHZ 7/7 + 16 RHZ 2/7; R.IV.: 4 RSHZP 7/7 + 20 RHZ 2/7. A la 24a semana de tratamiento, se registraron dos fracasos (0,6%), uno en el régimen III y uno en el régimen IV. Estos dos enfermos eran portadores de una cepa resistente.

Durante los 18 meses de seguimiento post-terapéutico, se registraron 10 recaídas (2,5%), de las cuales nueve eran cepas sensibles y siguieron siéndolo. Se registró un total de 12 (3,0%) fracasos recaídas después de dos años; siete en el régimen II, que no comportaba administración de pirazinamida; dos en el régimen III y tres en el régimen IV, con administración de pirazinamida durante cuatro semanas solamente. No se registró ninguna evolución desfavorable entre los enfermos del régimen I.

\* 40 Bd. Said Hamdine, Hydra-Argel, Argelia.

## COMPARACION DE DOS REGIMENES DE QUIMIOTERAPIA DE CORTA DURACION CONTRA LA TUBERCULOSIS PULMONAR EN TANZANIA.

*J.H. Darbyshire\*, S.J. Nkinda, A.J. Nunn, W. Fox y D.A. Mitchison*

Un régimen que comprende una fase inicial intensiva de dos meses de administración diaria de estreptomycin, isoniácida, rifampicina y pirazinamida (SHRZ), seguida por la administración de tioacetazona e isoniácida (TH) demostró ser altamente eficaz al ser utilizado durante ocho meses y aun fue efectivo cuando se administró durante seis meses. Debido al hecho de que la incidencia de toxicidad a la tiacetazona varía considerablemente según los países, existen muchos lugares donde no puede ser usada y donde no hay un medicamento barato de alternativa como acompañante de la isoniácida. Este estudio que se realiza en Tanzania compara dos regímenes quimioterápicos isoniácida y tiacetazona, o bien isoniácida sola, pretendiendo responder a la interrogante fundamental de si la isoniácida sola es adecuada luego de la fase

inicial de dos meses con cuatro medicamentos. El estudio incluyó 312 pacientes y los resultados comprenden las tasas de recaídas a los seis meses después de la suspensión del tratamiento. Se discutirán igualmente los hallazgos con respecto al rol de los medicamentos que acompañan a la isoniácida, provenientes de otros estudios hechos en Africa Oriental.

\* Medical Research Council, Tuberculosis and Chest Diseases Unit, Brompton Hospital, Fulham Road, Londres SW3 6HP, Reino Unido.

## TRATAMIENTO UNA VEZ POR SEMANA DE SUJETOS INACTIVADORES RAPIDOS DE LA INH, CON TUBERCULOSIS PULMONAR RECIENTEMENTE DIAGNOSTICADA, MEDIANTE UNA ASOCIACION MEDICAMENTOSA QUE CONTIENE INH-LENTA (ICN-CANADA). ENSAYO CLINICO CONTROLADO.

*J. Rogowski\*, J. Masztalerz, Z. Piasecki, y L. Eidus (fallecido)*

La quimioterapia administrada una vez por semana se ha mostrado eficaz en los inactivadores lentos de la INH, pero no en los inactivadores rápidos. El descubrimiento de una nueva rifampicina de acción prolongada (DL 475) podría constituir un tratamiento poderoso si la INH-Lenta fuera adecuada a una terapia una vez por semana de los inactivadores rápidos de la INH. El National Tuberculosis Research Institute de Varsovia, Polonia, en colaboración con el LCDC, Ottawa, Canadá, inició en 1979 un ensayo clínico controlado con el propósito de evaluar la eficacia y la importancia de los efectos secundarios de la INH-Lenta (ICN-Canadá). Se administró INH-Lenta en asociación con otros medicamentos, una vez por semana, durante nueve meses, después de un período inicial con INH, RFP y SM diariamente. Los inactivadores rápidos de la INH fueron asignados al azar a dos sub-grupos, uno tratado con INH-Lenta + RFP y otro con INH-Lenta + RFP = SM, una vez por semana. Los inactivadores lentos sirvieron de control y recibieron ya sea INH + RFP o bien INH + RFP + SM. Ciento veintiséis (126) enfermos fueron estudiados durante períodos hasta de tres años; —41 acetiladores rápidos y 85 lentos. En 96% de los enfermos se constató la negativización de la expectoración en tres meses. Los efectos secundarios se dieron con la misma frecuencia en los inactivadores rápidos y en los lentos. Estos efectos se observaron en 20 pacientes (11,4% del total de enfermos); sin embargo, sólo en tres casos (1,7%) fueron de gravedad tal que obligaron a modificar el tratamiento.

\* Instytut Gruźlicy, ul. Płocka 26, 01-138 Varsovia, Polonia.

## TUBERCULOSIS INFANTIL

### LA TUBERCULOSIS Y LA VACUNACION BCG EN ENFERMOS PEDIATRICOS: LA EXPERIENCIA DE MANITOBA.

*R. Pagtakhan\*, M. Thompson, F. Reis, M. Reed, C. Trevenen, T. Berg, A. Bensics, L. Bigornia, V. Chernick y E. Hershfield*

Se revisaron todos los casos (n = 552) de tuberculosis infantil (en menores de 16 años) vistos en Manitoba, Canadá,

entre 1968 y 1980. La tasa promedio de incidencia para la provincia era de 14 por 100,000, significativamente más elevada que la tasa correspondiente al total del país. La mayoría de los pacientes (75%) era de origen indio. Un tercio tenía antecedentes de vacunación con BCG, de los cuales 7,6% tenía una enfermedad grave, diseminada. La mayoría de los pacientes fueron detectados a través de la investigación de contactos (75%) y de tests rutinarios de Mantoux (11%). En más del 90% de los enfermos con formas pulmonares miliares, se observó a la radiografía un aumento de volumen de los ganglios paratraqueales. También se demostró la presencia de granulomas tuberculoides distribuidos en varios órganos, en 15 niños vacunados con BCG autopsiados en nuestro hospital (1977-1980), y que habían fallecido por otras causas. Se encontraron lesiones en el hígado (13 pacientes), pulmón (4), bazo (4), médula de los huesos (2) y endocardio (1). Así, a) la tuberculosis sigue siendo un problema importante de salud en los niños indios de Manitoba; b) la vacunación BCG no los protege completamente contra la forma diseminada de la enfermedad; c) la adenopatía paratraqueal concomitante es un elemento útil en el diagnóstico diferencial de la tuberculosis pulmonar miliar infantil; y d) la investigación de los contactos sigue siendo una herramienta muy importante en la detección de casos.

\* Children's Hospital, University of Manitoba, 685 Bannatyne Avenue, Winnipeg, Manitoba, Canada R2E 0W1.

#### LA TUBERCULOSIS INFANTIL EN SUECIA. UN ESTUDIO EPIDEMIOLOGICO SEIS AÑOS DESPUES DE HABERSE SUSPENDIDO LA VACUNACION GENERAL CON BCG DE LOS RECIEN NACIDOS.

V. Romanus\*

En 1975 se suspendió la vacunación general de los recién nacidos en Suecia. Una encuesta de tuberculosis en los niños realizada en este país desde 1969 a 1980 da cuenta de las consecuencias de esta medida. Se compara la morbilidad tuberculosa en seis cohortes de niños vacunados con BCG, nacidos en Suecia entre 1969 y 1974 y seis cohortes de niños no vacunados nacidos entre 1975 y 1980. Los grupos fueron observados entre 1969 y 1974 y entre 1975 y 1980, respectivamente. En las cohortes vacunadas con BCG se registraron 5 casos de tuberculosis pulmonar y 24 en las no vacunadas, lo que corresponde a tasas de 0,8 y 4,1 por 100,000 nacidos vivos, respectivamente. Entre los vacunados hubo un caso de meningitis y dos entre los no vacunados. Las cifras indican una eficacia de protección de la vacunación de BCG de alrededor de 80%. La tasa de morbilidad de tuberculosis en los niños no vacunados, nacidos en Suecia de padres extranjeros fue siete veces más alta que la de los niños no vacunados de padres suecos. Se observó también un aumento del número de casos de linfadenitis causadas por *Mycobacterium avium* en los niños no vacunados. Se registraron 81 casos de niños nacidos en 1975 o más tarde con linfadenitis a micobacterias no tuberculosas verificadas al cultivo, comparadas con tres casos en los niños vacunados con BCG y nacidos entre 1969 y 1974. El Dr. Il Sjogren, evaluará posteriormente estos resultados en comparación con aquéllos de la estimación del riesgo de infección tuberculosa predichos en 1975 para los niños no vacunados.

\* Epidemiological Department, National Bacteriological Laboratory, S-105 21 Estocolmo, Suecia.

#### NEUROTUBERCULOSIS, CON REFERENCIA ESPECIAL AL MANEJO DE LA MENINGITIS TUBERCULOSA (TBM) EN EL NIÑO.

P.M. Udani\* y D.K. Dastur

La tuberculosis representa un problema de salud mayor en los países en vías de desarrollo. Se estudiaron más de 600 casos de diversos tipos de neurotuberculosis, siendo la meningitis tuberculosa (TBM) con encefalopatía edematosa la forma más frecuente. Los otros tipos encontrados con menos frecuencia fueron la TBM serosa, la TBM espinal, con o sin mielopatía, la polineuritis y la neuropatía periférica. La letalidad por TBM era de 100% en la era prequimioterápica, de 80% entre 1946 y 1953, de 50% de 1954 a 1970 y de 10-15% desde 1971. Hoy en día, los resultados son mejores gracias a un mejor conocimiento de la patología y de los mecanismos patogénicos, así como a la existencia de medicamentos altamente eficaces. Los elementos más importantes en el manejo de estos casos son los siguientes: la precocidad en el diagnóstico de las diversas formas de TBM, la utilización de por lo menos cuatro drogas quimioterápicas, la rifampicina (RMP), la isoniacida (INH), la pirazinamida (PZ) y la estreptomycin (SM) o el etambutol (ETH) durante los tres o cuatro primeros meses, la RMP, la INH, el ETH en el segundo período de tres a cuatro meses, y la INH y el ETH durante los tres a cuatro últimos meses, con dexametasona durante dos a tres meses. El diagnóstico precoz de la hidrocefalia en particular por medio del scanner y el tratamiento por shunt V.A. han mejorado el pronóstico. Se presentarán los resultados de diversas modalidades terapéuticas y, de paso, se mencionarán los cuadros clínicos modificados de la TBM, ya sea por una quimioterapia inapropiada, por la vacunación BCG o por ambos. Sin embargo numerosos problemas en el manejo de las complicaciones son todavía un desafío para el pediatra y los especialistas de otras disciplinas.

\* Profesor Emeritus, Institute of Child Health, Sir J.J. Group of Hospitals, Grant Medical College, and Hon. Pediatrician, Bombay Hospital, Bombay, India.

#### QUIMIOTERAPIA DE CORTA DURACION EN NIÑOS, DOS AÑOS DE SEGUIMIENTO.

H.B. Dingley\*

Ciento veinticuatro (124) niños de 6 meses a 14 años de edad con manifestaciones primarias y post-primarias de tuberculosis fueron asignados al azar a cuatro esquemas de tratamiento: A) INH + PAS + tioacetazona; B) INH + pirazinamida + etambutol; C) INH + pirazinamida + rifampicina; D) INH + tioacetazona. La duración del tratamiento fue de 26 semanas para los tres primeros esquemas y de 78 semanas para el cuarto. Todos los niños fueron seguidos durante 104 semanas. Sólo seis niños tenían frotis positivos al comienzo del estudio y sólo uno de ellos no se negativizó al final del tratamiento. Dos enfermos fallecieron en los grupos A, B y C. Los síntomas de toxicidad fueron insignificantes en todos los grupos. La respuesta radiológica fue satisfactoria en todos los esquemas y la mejor fue la del esquema con rifampicina.

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## TUBERCULOSIS EXTRA-PULMONAR

### ADMINISTRACION PARENTERAL DE RIFAMPICINA EN PACIENTES CON MENINGITIS TUBERCULOSA (RESULTADOS PRELIMINARES)

*M. Kissling\* y M. Xilinas*

Se ha producido una forma inyectable de la rifampicina (RMP), dada la dificultad que puede existir en el tratamiento por vía oral de los pacientes con meningitis tuberculosa. Hasta ahora, 29 pacientes con meningitis tuberculosa han sido tratados por vía parenteral, 18 adultos (18 a 21 años de edad) y 11 niños (1 a 12 años de edad). La RMP fue administrada en inyecciones endovenosas o en gota a gota endovenoso, con INH y/o estreptomycin. Las dosis diarias de RMP fueron entre 300 a 600 mg en los adultos y de 15-30mg/kg de peso en los niños, por períodos superiores a 31 días. La concentración de RMP en el LCR fue de alrededor de 13% de la encontrada en el plasma después de las primeras tres horas de fleboclisis. Se discutirán otros datos sobre la farmacocinética del producto. En 27 pacientes se obtuvieron resultados sobre la eficacia del tratamiento, 20 de los cuales mostraron una mejoría clara. Cuatro de los 29 pacientes presentaron efectos inesperados: ictericia (2), exantema (1) dolor post inyección (1), cuya relación con el tratamiento con RMP no siempre fue establecida. La RMP por vía parenteral aumenta las posibilidades de evolución favorable de los pacientes con meningitis tuberculosa.

\* Ciba-Geigy Ltd., Med., Dept., Basilea, Suiza.

### QUIMIOTERAPIA Y QUIMIOTERAPIA COMBINADA CON CORTIESTEROIDES EN EL TRATAMIENTO DE LA TUBERCULOSIS MILIAR AGUDA EN ADOLESCENTES Y ADULTOS.

*Sun Tung-nien\**

Se comparan los resultados de la quimioterapia y de la quimioterapia combinada con corticoesteroides, en 55 casos de tuberculosis miliar aguda en adultos y adolescentes. Se registraron siete muertes (12,7%), pero el porcentaje de casos fatales fue más alto (18%) en el grupo uno, tratado con antibióticos solamente, que en grupo dos, tratado con una combinación de antibióticos y corticoesteroides (7,4%). La acción de los corticoesteroides en el tratamiento consiste en ayudar a los pacientes a superar el stress de la infección que lo invade, a disminuir los síntomas tóxicos y la reacción exudativa no específica en los focos tuberculosos, de manera que las drogas antituberculosas puedan difundir libremente en las lesiones para ejercer su acción bactericida. La quimioterapia debió continuarse durante 18 a 24 meses, pero los corticoesteroides fueron administrados durante los tres a los seis primeros meses. De los 48 pacientes dados de alta del hospital en buenas condiciones, durante los últimos 20 años, 33 seguían viviendo en Shanghai y estaban todos probadamente curados desde el

punto de vista clínico. Quince (15) pacientes continuaron su tratamiento en otras provincias después del alta hospitalaria y no fueron seguidos.

\* The Shanghai Second Medical College, Zhong Quing Nan Lu, Shanghai, China.

### QUIMIOTERAPIA DE SEIS MESES EN LA TUBERCULOSIS UROGENITAL

*V. Skutil\*, J. Varsa, M. Obsintník e I. Moro*

El estudio comprende 13 pacientes con tuberculosis urogenital bacteriológicamente confirmada y no tratada anteriormente. Se aplicó un esquema con: RIF 600 mg + INH 300 mg + PZA 1,000 mg administrado diariamente en el hospital durante cuatro meses. Se llevaron a cabo intervenciones quirúrgicas de reparación y extirpación hacia el final del 2º mes de tratamiento. La terapia fue completa en 106 pacientes (93,8%). En 83% de ellos los cultivos se hicieron negativos en el 1er. mes, y en 98.1% en el 2º mes. Al final del sexto mes los cultivos de orina del total de 106 pacientes eran negativos. No se observaron fracasos de la quimioterapia en el curso del tratamiento ni recaídas bacteriológicas en el período de seguimiento de seis a 30 meses después de completada la quimioterapia. Se observaron reacciones adversas en 11 de los 113 pacientes; en siete de ellos se suspendió el tratamiento: debido a reacciones hepatotóxicas en cinco (GPT más de 70 u/l) a artralgias en uno y debido a un exantema en otro.

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### TRATAMIENTO DE LA TUBERCULOSIS EXTRAPULMONAR CON QUIMIOTERAPIA DE CORTA DURACION.

*A.K. Dutt\*, D. Moers y W.W. Stead*

La quimioterapia de corta duración (QCD) con isoniácida (INH) y rifampicina (RIF) es altamente eficaz en la tuberculosis pulmonar. Sin embargo, no se conoce bien el resultado de este tipo de quimioterapia en la tuberculosis extra-pulmonar (TEP). Tratamos 134 enfermos con TEP con 300 mg de INH y con RIF diariamente durante un mes, en seguida, INH 900 mg y RIF 600 mg dos veces por semana durante otros ocho meses en un servicio de tratamiento de terreno en el Departamento de Salud de Arkansas. Las localizaciones de la enfermedad eran: ósteo-articulares: 23; diseminadas: 13; meningitis: 8; génito-uritarias: 13; pericardio: 7; abdominales: 8; linfáticas: 16; pleurales: 37 y diversas: 9. La edad promedio de los pacientes era de 55,4 años. En 99 casos (74%) la enfermedad había sido confirmada por la bacteriología y/o la histología. Tres pacientes presentaron efectos colaterales importantes: hepatitis en dos y "síndrome gripal" en uno. De los 134 pacientes, 89 completaron totalmente la quimioterapia y en ellos no se observó recaídas durante un período que varió entre seis y 55 meses. Sin embargo cuatro pacientes murieron durante el tratamiento: dos de ellos con tuberculosis miliar. Así, se obtuvo un éxito en el 97% de los pacientes que completaron el tratamiento. Durante el mismo período fueron tratados 90 pacientes con el esquema convencional de 18-24 meses; 81 completaron el tratamiento. Se registró una sola recaída

durante el seguimiento. De esta manera, se puede concluir que la QCD es tan efectiva para la tuberculosis extrapulmonar como para la tuberculosis pulmonar. El esquema utilizado en Arkansas tiene las siguientes ventajas: acortar el tratamiento, disminuir las dosis, reducir el costo, y facilitar la supervisión.

\* Veterans Administration Medical Center, 300 E. Roosevelt, Little Rock AR. 72206, Estados Unidos.

#### ESTUDIO DEL HONG KONG CHEST SERVICE/BRITISH MEDICAL RESEARCH COUNCIL DE UN PROGRAMA DE QUIMIOTERAPIA ENTERAMENTE SUPERVISADA PARA LA TUBERCULOSIS PULMONAR, ADMINISTRADA UNA VEZ POR SEMANA EN LA FASE DE CONTINUACION EN UN AREA RURAL DE HONG KONG.

*S.H. Tsang, D. Lum, S.L. Chan, W.G.L. Allan, N.J.C. Snell y A.J. Nunn.*

La política del Chest Service, en lo referente a la quimioterapia de la tuberculosis pulmonar, en las áreas urbanas de Hong Kong, es de dar cada dosis bajo estricta supervisión, tratándose de enfermos ambulatorios. Esto no ha sido posible en las áreas rurales donde los pacientes eran tratados con un esquema diario con isoniácida y PAS suplementado con estreptomycin en la etapa inicial, pero autoadministrado en la fase de continuación que duraba 18 meses. En mayo de 1979, se comenzó un programa de quimioterapia enteramente supervisado en base a un esquema con estreptomycin, isoniácida, rifampicina, pirazinamida y etambutol (SHRZE) diariamente durante un período inicial de dos meses en el que el paciente permanecía hospitalizado, seguido de un tratamiento ambulatorio con estreptomycin, isoniácida, rifampicina y etambutol (SHRE) dados una vez por semana bajo estricta supervisión, siendo la duración total de la quimioterapia de 12 meses.

Aproximadamente 300 pacientes por año cumplen con los requisitos para ser admitidos en el programa. Se presentarán los resultados sobre 300 pacientes después de 18 meses de terminado el tratamiento, sobre 450 después de 12 meses y sobre 600 después de seis meses.

\* Yaumati Chest Clinic, Lowloon, Hong Kong.

#### RESULTADOS DE UN PROGRAMA DE QUIMIOTERAPIA DE CORTA DURACION DE LA TUBERCULOSIS, APLICADO EN PRACTICA DE RUTINA

*P. Iturbe\*, H.S. Morales y R. París*

En 285 casos de tuberculosis pulmonar bacteriológicamente confirmada se aplicó un régimen diario de cuatro drogas durante dos meses, seguidos de una fase intermitente con tres drogas durante cuatro meses (2SHRZ/4S<sub>2</sub>H<sub>2</sub>Z<sub>2</sub>). Este régimen fue adoptado para el tratamiento de todo caso nuevo descubierto; por consiguiente, se aplicó en práctica de rutina, dentro de las condiciones operativas del programa integrado de tuberculosis, o sea en forma ambulatoria y completamente supervisada. Sólo en 2,45% de los casos hubo que cambiar el régimen por toxicidad.

Hubo 14% de abandonos, cifra mayor que la encontrada en evaluaciones anteriores, debido a fallas ocurridas en la supervisión. En nuestra experiencia el factor que más ha influido sobre los abandonos es la organización y los aspectos operacionales del tratamiento, más que el régimen quimioterápico.

Se comprobó la rapidez de la acción bactericida; 96,5% de los casos fueron negativos al 2º mes y 100% al 40. mes, así como también la eficacia de la acción esterilizante: sólo se produjo una (1) recaída (0,4%). El tiempo de observación post-tratamiento fue de seis a 24 y más meses (42 casos de seis a 12 meses y 196 casos de 12 a 24 y más meses).

\* Hospital General del Sur, Maracaibo, Venezuela.

#### ESTUDIO DE AGRA SOBRE LA QUIMIOTERAPIA AMBULATORIA MAS CORTA, ACEPTABLE Y EFICAZ POSIBLE DE LA TUBERCULOSIS PULMONAR, SEGUIMIENTO DURANTE DOS AÑOS.

*M.L. Mehrotra\*, G.K. Dutt y C.C. Kant*

Se informa sobre los resultados de 360 pacientes sometidos a ensayos terapéuticos controlados en el Tuberculosis Training Center y en el Chest Institute de Agra. En dos regímenes de cuatro meses y medio (3RSZH/RH, 3RSZH/H<sub>2</sub>S<sub>2</sub>Z<sub>2</sub>) y en un régimen de tres meses (3RSZH) se utilizaron los cuatro medicamentos antituberculosos más potentes: isoniácida, rifampicina, pirazinamida y estreptomycin. Un 90% de los pacientes cumplió con la toma de sus medicamentos; el tratamiento fue ambulatorio desde el primer día. Se exigió la asistencia al consultorio externo para la administración de los medicamentos. Al cabo de tres meses, la esterilización bacteriológica fue obtenida en el 100% de los pacientes. El seguimiento durante un año mostró una tasa de recaídas del 2% en los dos regímenes de cuatro meses y medio y del 6% en el régimen de tres meses.

Se observaron efectos secundarios en 16% de los pacientes, principalmente durante las primeras ocho semanas. La aparición de toxicidad requirió la suspensión del tratamiento en un 4,3% de los pacientes y en el 12% restante las reacciones secundarias fueron controladas fácilmente. El análisis preliminar de dos años de seguimiento muestra una estabilidad de los resultados obtenidos un año después de la suspensión del tratamiento.

Se presentará también la acción del tratamiento sobre los niños nacidos de madres tuberculosas que recibían quimioterapia de corta duración.

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## PROFILAXIS DE LA TUBERCULOSIS

### CONTROL BIOQUIMICO DURANTE LA TERAPIA PREVENTIVA CON ISONIACIDA

W.J. Alexander\*, J.G. Housch y W.L. Roper

Se realizó una evaluación prospectiva de 141 pacientes que recibían isoniácida (INH) entre el tercer y el sexto mes de tratamiento. Se hizo una determinación única de transaminasas glutámicoxalacética (SGOT) para cada paciente asintomático, 4,3 meses en promedio después del comienzo del tratamiento. Se encontraron niveles de SGOT iguales o superiores al doble de la normal en: 12,5% de los pacientes del grupo de edad 35-44 años; 21% del de 45-54 años; 6% del de 55-64 años; 8% del de 65-74 años; y 13% de de 75-84 años. La necesidad de una terapia preventiva con INH fue reconsiderada en ocho pacientes (5,6%) que tenían niveles de SGOT iguales o superiores a cuatro veces normal. Durante el período de seguimiento de esta cohorte de pacientes no se registraron casos de hepatitis evidentes desde el punto de vista clínico.

Concluimos que una sola determinación del nivel de SGOT efectuada tres a seis meses después del tratamiento con INH puede ser un indicador útil de la hepatotoxicidad potencial en pacientes que toman este medicamento. Esta determinación bioquímica puede ser realizada en la mayoría de los servicios locales de salud que ofrecen un tratamiento preventivo con INH.

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### TRATAMIENTO PREVENTIVO DE LA TUBERCULOSIS.

F. van der Kuyp\*, J.P. McCollough y T.M. Daniel

La profilaxis con isoniácida (INH) es la única herramienta disponible para prevenir el desarrollo de la enfermedad activa en los individuos infectados con bacilos tuberculosos. La mayor dificultad estriba en su asociación con la toxicidad hepática de la cual han dado cuenta algunos autores. Nuestra experiencia se basa en la profilaxis con INH en 10 244 sujetos, de los cuales 30,4% tenían menos de 20 años de edad, 42,0% entre 30 y 49 años y 27,6% 50 años o más. La dosis de INH era de 10 mg por kg de peso, con dosis máxima de 300 mg, diariamente, entregada mensualmente y durante un año. Los análisis de sangre para estudiar la toxicidad hepática se realizaron siempre que había síntomas sospechosos. Se constataron efectos laterales que obligaron a suspender la INH en 8,1% de los casos. La mayoría fueron sin consecuencias. Se observó una hepatitis en 56 casos (0,55%); el 60% de éstas se desarrolló dentro de las ocho primeras semanas. Los criterios para el diagnóstico de hepatitis fueron: SGOT (transaminasa glutámica oxalacética) 250 u. y/o SGPT (transaminasa glutámica pirúvica) 100 u. y/o bilirrubina total 2,5% mg %. La fre-

cuencia de la hepatitis fue desde 0 (cero) en los menores de 20 años hasta 9,6 por 1 000 en los sujetos de 50 años y más. No hubo muertes atribuibles a la hepatitis.

Concluimos que, con un manejo apropiado, la profilaxis con isoniácida es relativamente inocua y que su aplicación amplia merece ser considerada.

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### RESULTADOS DEL SEGUIMIENTO DE CASOS DE LESIONES FIBROTICAS CON TERAPIA PREVENTIVA CON ISONIACIDA. ESTUDIO DE LA UICT.

A. Krebs\*

Los resultados del seguimiento durante ocho años, provenientes de cuatro países participantes (más de 21,000 personas incluidas) y durante 10 años en un país (11,700 sujetos) muestran que: en las personas con lesiones fibróticas el riesgo de activación permanece estable pero la tasa anual disminuye considerablemente en los últimos años; el tratamiento preventivo de 12 semanas es efectivo sólo temporalmente; el tratamiento de 24 semanas es, en general, casi tan efectivo como el de 52 semanas; la relación beneficio/riesgo es más favorable con el esquema de 24 semanas en cualquier momento de la evolución.

Se deberán discutir las medidas para obtener una relación-riesgo aún mas satisfactoria.

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### CAUSAS Y SIGNIFICADO DIAGNOSTICO DE LA HEMOPTISIS EN LA ACTUALIDAD.

B. Mariani\*

Las investigaciones efectuadas por el Profesor Omodei Zorini en el Instituto Forlanini en 1934 demostraron que la hemoptisis tenía por origen la tuberculosis pulmonar en el 91% de los casos. El 9% restante era debido a la bronquiectasia y a la insuficiencia cardíaca. En 1962 realizamos una amplia investigación al respecto, que reveló una tuberculosis en 62% de los casos, bronquiectasia en el 24% y cáncer del pulmón en el 2%.

Según los últimos estudios realizados en el Instituto Forlanini en 1980, la mayoría de las hemoptisis eran causadas por el cáncer del pulmón (40,9%), luego seguía la bronquiectasia (23,3%) y después la tuberculosis pulmonar (15,23%); las otras hemoptisis (19,1%) tenían como causa otras neumopatías (neumonías, bronquitis, absceso pulmonar, neumooniosis y, raramente otras enfermedades).

El autor realza las diferencias importantes del valor diagnóstico de la hemoptisis observadas en encuestas realizadas en Italia en épocas diferentes y las atribuye a los cambios epidemiológicos y clínicos ocurridos en el último tiempo en el dominio de las enfermedades respiratorias.

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# ESTUDIOS DEL HONG KONG, CHEST SERVICE / TUBERCULOSIS RESEARCH CENTRE MADRAS / BRITISH MEDICAL RESEARCH COUNCIL SOBRE LOS CASOS DE TUBERCULOSIS PULMONAR NEGATIVOS A LA MICROSCOPIA DIRECTA.

S.L. Chan\*

En lo que se refiere a los pacientes con tuberculosis pulmonar radiográficamente "activa" pero cuyos frotis y cultivos son negativos, no se sabe con certeza quiénes requieren tratamiento, y entre los que lo necesitan, cuál debe ser la duración adecuada. No está tampoco establecida la duración apropiada de la quimioterapia de los enfermos con frotis comprobadamente negativos pero con cultivo positivo. Se informa sobre los resultados de dos estudios correlacionados. En el primer estudio se incluyen 1,212 pacientes que fueron distribuidos al azar entre los siguientes grupos: 1) QS: quimioterapia selectiva; la terapia antituberculosa no se comenzó antes de confirmar la actividad tuberculosa 2) 2SHRZ: estreptomina, isoniacida, rifampicina y pirazinamida, diariamente durante dos meses 3) 3SHRZ: igual que 2) pero durante tres meses 4) esquema estándar de 12 meses. Se presentan los resultados finales del total de la población después de cinco años. En el segundo estudio, se trataron pacientes con cultivos negativos con SHRZ diariamente durante tres meses o tres veces por semana durante ya sea tres o cuatro meses, y pacientes con cultivos positivos diariamente durante cuatro meses y tres veces por semana durante cuatro o seis meses. Se presentaron los resultados, al cabo de 12 meses para alrededor de 1,500 pacientes.

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# INCIDENCIA DE LA TOXICIDAD OFTÁLMICA EN PACIENTES QUE RECIBEN REGIMENES QUE CONTIENEN ETAMBUTOL EN EL TRATAMIENTO DE LA TUBERCULOSIS PULMONAR.

K Mohanty\*, R. Sundrani y D. Kulkarni

Se estudió la incidencia de la toxicidad oftálmica en 290 pacientes que reciben etambutol como medicamento de primera línea o de reserva con distintos tipos de posología, para el tratamiento de la tuberculosis pulmonar: el 8,2% de los pacientes presentó una toxicidad oftálmica de intensidad variable. La incidencia máxima de toxicidad oftálmica se observó en los enfermos de menos de 15 años de edad y en los que recibieron las dosis más altas de etambutol (p. ej. 25 mg/kg de peso). Los casos de toxicidad ocular se observaron con más frecuencia en los tres primeros meses de tratamiento, independientemente de que el etambutol hubiera sido usado como medicamento de primera línea o de reserva. Al suspender el medicamento se observó una regresión completa de los signos y síntomas de toxicidad.

\* Tuberculosis & Chest Diseases Department, Grant Medical College & Sir J.J. Group of Hospitals, Bombay 8, India.

# ACCION DE LA PIRAZINAMIDA SOBRE EL HIGADO DE PACIENTES TUBERCULOSOS. ESTUDIO ESTRUCTURAL.

J.A. Pilheu\*, M.C. de Salvo, O. Koch y R. Arias

Catorce (14) pacientes tuberculosos sin tratamiento previo recibieron Pirazinamida (Z) en diferentes formas: siete la recibieron sola, durante 15 días; siete en asociación con INH, RAMP, SM. Un grupo control (cinco pacientes) recibió INH, RAMP, SM, EMB. A todos se les efectuó una biopsia hepática (BH) antes de recibir las drogas y se la estudió con microscopía de luz. Después de recibir Z sola 15 días, y las asociaciones (INH, RAMP, SM, Z y INH, RAMP, SM, EMB) durante dos meses, se repitió la BH y se la estudió con microscopía electrónica (ME). En los pacientes que recibieron Z sola, la ME fue normal en tres casos y en los cuatro restantes había megamitocondrias (MM) en dos casos, hiperplasia del retículo endoplásmico liso (REL) en tres casos y cuerpos paracrystalinos (CP) en tres casos. (En los que recibieron INH, RAMP, SM, Z, hubo agrandamiento de las mitocondrias en tres casos, MM en un caso, hiperplasia del REL en cinco casos, CP en dos casos. En aquéllos que recibieron INH, RAMP, SM, EMB, hubo uno normal, agrandamiento mitocondrial en un caso, MM en un caso, hiperplasia del REL en un caso, CP en dos casos y dilatación del RE rugoso en un caso. Las alteraciones encontradas son inespecíficas y no atribuibles a la Z con exclusividad.

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# Medicolegal Decisions



## **SURGERY PATIENT RECOVERS DAMAGES AGAINST PHYSICIANS**

A trial court did not err in refusing to instruct a jury as to primary and secondary liability of two physicians, a Pennsylvania appellate court ruled.

A patient consulted her gynecologist because of excessive bleeding. He recommended and performed a hysterectomy. During the operation, profuse bleeding occurred, and the gynecologist sent for a cardiovascular surgeon. Both physicians attempted to ligate the arteries involved.

In the course of the surgery, a ureter and kidney were damaged. After the operation, the blood supply was diminished to the patient's right leg, which subsequently was amputated above the knee. The patient's kidney, which appeared perforated, was removed later.

The patient sued the hospital, the gynecologist, the cardiovascular surgeon, and an associate of the cardiovascular surgeon, alleging that negligent performance of the operation and negligent postoperative care resulted in loss of her kidney and leg. At the trial, experts testified that other surgical procedures could have reduced the risk of harm to the leg. The cardiovascular surgeon left for vacation less than a week after the operation, and his associate was not called on the case by the gynecologist until, in his opinion, irreversible damage had occurred.

The court rendered judgment on a jury verdict for the patient and her husband. The patient was awarded \$500,000, and the husband was awarded \$50,000 against the gynecologist and the cardiovascular surgeon. The hospital and the associate of the cardiovascular surgeon were exonerated by the jury.

On appeal, the cardiovascular surgeon contended that the lower court's charge on causation for post-operative care in effect directed a verdict against him, even though such words were not specifically used. The appellate court disagreed. The court found that when taken in the context of the charge as whole, the lower court's charge was merely an explanation of the patient's burden of proof on the issue of causation.

The gynecologist contended that the trial court erred in refusing to instruct the jury as to primary and secondary liability between him and the cardiovascular surgeon. He contended that the court should have distinguished injuries of the

leg from those involving the kidney and ureter and awarded damages accordingly. The appellate court disagreed. The court said that the issue was not primary versus secondary responsibility but whether the gynecologist fell below the standard of care in his duties owed to the patient. The jury found that both physicians were responsible for the patient's loss of her leg and kidney.

The appellate court affirmed the lower court's judgment. —*Hoeke v. Mercy Hospital of Pittsburgh*, 445 A 2d 140 (Pa. Super. Ct., April 30, 1982).

## **PHYSICIANS SUED FOR ALLEGED UNNEEDED CHOLECYSTECTOMY**

A trial court erred in granting summary judgment for a physician whose diagnosis of cholecystitis was allegedly negligent, a Georgia appellate court ruled.

The physician recommended removal of a patient's gallbladder to cure certain gastrointestinal symptoms including nausea, vomiting, abdominal and stomach pain, and intestinal and bladder spasms. The gallbladder was removed by a surgeon after consultation, but the patient contended that her symptoms continued until she went to another physician for treatment. She filed suit for the alleged improper removal of her gallbladder.

The physician moved for summary judgment based on affidavits by himself and the surgeon who performed the operation. The patient offered an affidavit of an expert witness who said that the diagnosis of cholecystitis was improper, the diagnosis was incomplete, and the surgery was unnecessary.

Reversing the trial court's grant of summary judgment for the physician, the appellate court said that the case presented a jury question. There was a substantial fact issue raised by the physician's affidavits, and the issue must be decided by a jury, the court said. —*Jones v. Myers*; 291 S.E. 2d 394 (Ga. Ct. of App., May 11, 1982).

## **PHYSICIAN SUED FOR ALLEGED NEGLIGENCE IN CARE OF CORONARY OCCLUSION**

The estate of a patient who died of coronary occlusion after being X-rayed at a hospital was entitled to a new trial against a physician because of prejudicial errors during the trial, a New York appellate court ruled.

The patient first saw the physician in October 1970. He had both premature ventricular atrial contractions. His

father died of a coronary at the age of 54 and his mother had hypertension. A year later the patient returned, complaining of pain in the precordium and substernum regions. The physician prescribed Valium and Sorbitrate. On his next visit, in April 1972, the physician prescribed Inderal and discovered that the patient had an abnormally high cholesterol level.

Two months later, the patient was cleared for knee surgery, but the physician refused to clear the patient for further surgery in January 1974 because of abnormal wave patterns on a cardiogram. However, the physician did not consider his patient to be suffering from heart disease at that time.

In November 1974, the patient complained of pressure in his chest and left arm and told the physician that his mother had recently died of a massive coronary. The patient had no other common symptoms of heart disease, such as weakness, sensations of heat or cold, sweat or difficulties in breathing. An electrocardiogram revealed no evidence of myocardial infarction.

On January 10, 1976, the patient had another EKG, which was normal. Six days later the patient called the physician from work. he complained of aches and burning sensations in his upper chest, shoulder blades, and back. The physician instructed the patient to drive to a hospital for an X-ray of the cervical and dorsal spine. He did so, and on the way home, he died of coronary occlusion.

A trial court dismissed a complain against the hospital, and a jury returned a verdict for the physician. Reversing the judgment for the physician, the appellate court said that several prejudicial errors were committed during the trial. The court had erred in excluding a hospital record that contained the medical history recorded by the physician who treated him for his knee injury. The excluded portions were clearly relevant to the issue of whether the physician had notice of the patient's coronary condition.

The trial court erred in restricting questioning of the defendant physician and not permitting him to be questioned as a medical expert. The case was remanded for a new trial of the claim against the physician. —*Segreti v. Putnam Community Hospital*, 449 N.Y.S. 2d 785 (N.Y. Sup. Ct., App. Div., May 3, 1982).

#### NO NEGLIGENCE IN CARE OF INNER EAR PROBLEM

There was sufficient evidence for the jury to find that a physician was not negligent in the diagnosis and treatment of a patient's condition, a Louisiana appellate court ruled.

The patient had suffered from bouts of vertigo since before 1973. The episodes were sometimes so severe that he would fall to the floor with vomiting and nausea. The condition affected his job performance as an insurance salesman who had to drive a car.

In February 1976, a physician who had been treating the patient for heart problems sent him to the physician for evaluation of vertigo. The physician performed an audiogram, a tympanogram, and an electronystagmogram, finding that the patient's right ear showed definite lack of function. He suspected a tumor on the eighth nerve and had the patient admitted to a hospital for tests by a neurosurgeon. The neurosurgeon

made a diagnosis of eighth nerve dysfunction but found no tumor.

The physician further tested the patient in March 1976, concluding that he was suffering from Meniere's disease, an inner ear disorder. In April, after obtaining the patient's consent, he performed endolymphatic shunt surgery, with the result that the patient lost the hearing in his right ear.

The patient sued the physician for malpractice, contending that the operation performed was not the proper treatment for his condition and that the physician failed to inform him that it might result in total and permanent hearing loss. He said that had he been informed of the risk he would not have consented to the surgery but would have chosen other methods of treatment.

At the trial, an expert in neurotology testified that the shunt procedure was standard treatment for recurrent and intractable vertigo. All experts who testified agreed that the purpose of the shunt surgery was to eradicate the vertigo and preserve the hearing. The physician testified that the patient, who had incapacitating vertigo that did not respond to treatment, pleaded with him to do something to help him. The patient testified that his vertigo had improved, if not cleared up, after the operation. The jury decided for the physician.

On appeal, the court found that there was sufficient credible evidence on which the jury could reasonably base its findings in favor of the physician. The court affirmed findings in favor of the physician. —*Davidson v. Peden*, 413 So. 2d 568 (La. Ct. of App., April 13, 1982).

#### NO NEGLIGENCE IN MD'S TREATMENT OF MENINGITIS

A father's telephone conversations with a nurse were admissible in a malpractice suit, a California appellate court ruled.

According to his parents, the patient, an 8-week-old baby, awoke on a Friday morning with a rectal temperature of 103°F. The mother talked to a physician's nurse, who in turn talked to the physician about the child's condition. On Saturday, the mother talked with the physician, and on Sunday to a physician who was taking the first physician's calls. On Monday, the mother took the baby to the physician's office, and a diagnosis of bacterial spinal meningitis was made.

The parents sued the physicians for malpractice, contending that the symptoms allegedly described by the mother to the physicians and nurse should have led them to suspect meningitis before Monday. Expert witnesses for both sides agreed that, given the facts as testified to by the mother, the physician's conduct was below the standard of care for a general family physician.

According to the nurse, the mother stated that the baby had a temperature of 100°F. but no other symptoms. The physician had no memory of the telephone calls, but he agreed that if the mother's report was correct he should not have prescribed drugs without seeing the child. He agreed that a newborn infant with meningitis should be treated immediately. Testimony indicated that laboratory tests of the baby were incompatible with the mother's account of the child's symptoms over the weekend. The jury decided for the physicians.



On appeal, the parents contended that the father's conversations with a nurse friend were not admissible in evidence. The father had talked to the nurse on the Saturday of the critical weekend with regard to the child's symptoms and his and the mother's care of the infant and their other children. A second phone conversation with the nurse took place three years later, shortly before trial. The court found that the conversations were admissible, pointing out that the nurse would have been able to understand the significance of and remember better than the father his statements made during the critical weekend. The court said that the jury showed by their verdict that they believed her testimony.

The court also found that evidence of habit and custom could be introduced to show that the physician and his staff habitually asked that an infant with a temperature of more than 100°F. be brought in for an examination. The court affirmed the trial court's judgment. —*Dincau v. Tamayose*, 182 Cal. Rptr. 855 (Cal. Ct. of App., May 18, 1982).

**PHYSICIAN NOT NEGLIGENT IN CARE  
OF HAND INJURY**

A trial judge did not err in permitting orthopedic surgeons to testify with regard to the cause of a patient's clenched hand, the highest court of Massachusetts ruled.

The patient's hand was injured while she was attending school. A physician placed a circular plaster cast on her arm from her fingers to her elbow. Three days later, her fingers were blue, swollen, and cold. The physician replaced the cast with one of a different kind. After three more days, the fingers were still blue and swollen and started to "claw up," and the physician recommended an operation.

The patient's parents took her to another physician, and she was hospitalized for five days of observation and physical therapy. She was hospitalized several more times, but only after an operation almost three years later was her hand permanently unclenched.

The patient sued the first physician for malpractice. At the trial, there was a substantial dispute as to whether the patient's clenched hand was caused by the tightness of the cast or by circumstances unrelated to any physical injury, or at least an injury caused by the physician.

A medical witness for the patient testified that the type of cast first applied was inappropriate and too tight, that the physician did not supervise the patient adequately, and that the clenched hand was due to his negligence. An orthopedic surgeon testifying for the patient said on cross-examination that there was a psychological element to the problem, that the fingers could be straightened under anesthesia, and that the physician had not caused the patient serious physical injury. Two orthopedic surgeons testifying for the physician said that the clenched hand was not the product of a physical injury but of a psychological problem. The jury decided for the physician.

On appeal, the highest court of Massachusetts affirmed the decision. The trial judge did not err in permitting the orthopedic surgeons to testify as to a psychological basis for the clenched hand; the surgeons were qualified to express their opinions and they had seen similar cases in which a clenched hand was the result of a psychological disorder, the court said.

The court pointed out that they did not testify as to the cause of the psychological disorder but as to the absence of a direct physical cause.

The patient also contended that the judge should not have denied her request to present a rebuttal witness at the close of the physician's case. The appellate court found that the judge did not abuse her discretion where the witness's testimony would have introduced a new theory of causation. —*Drake v. Goodman*, 434 N.E. 2d 1211 (Mass. Sup. Jud. Ct., May 3, 1982).

**MD'S MEDICAL EDUCATION NOT  
COMMUNITY PROPERTY**

A physician's medical education was not community property nor individual property and was not subject to division in a divorce proceeding, a California appellate court ruled.

The physician filed for divorce after about ten years of marriage. At the time of trial his wife was earning about \$26,400 per year. The court noted that there was not one shred of evidence before the trial court to demonstrate that the case was one where the wife had "put Hubbie through" medical school as was widely represented in the media. The trial court entered a joint custody order, awarded the wife \$250 per month child support, reserved jurisdiction over a request for spousal support for five years, and awarded her \$1,250 in attorney's fees and costs.

On appeal, the court said that its earlier opinion stated that the husband's enhanced earning capacity was property subject to division. Upon further reflection, the court said that its premise for that opinion was wrong. The husband's professional education had none of the attributes of community or separate property. The wife was entitled to no part of his enhanced earning power and in fact was not entitled to an award of spousal support.

The trial court's decision was affirmed, except as to the wife's request for \$800 for her expert witness. She was ordered to pay that amount herself. —*In re the Marriage of Sullivan*, 184 Cal. Rptr. 796 (Cal. Ct. of App., Aug. 2, 1982).

*Editor's Note:* A prior decision in this case was reported in THE CITATION, Vol. 45, No. 1, p. 5.

**STATE HOSPITAL MUST ACCEPT ALL  
PATIENTS EVEN IF OVERCROWDED**

A state hospital's evaluation and treatment facility was required by law to accept all persons presented by county mental health professionals within its allotted area, whether or not such acceptance would overtax its facilities, the Washington Supreme Court ruled. The hospital contended that it was not obliged to accept patients if all the beds in the facility were occupied. The court said that according to law, as a facility providing 72-hour evaluation and treatment, the hospital's evaluation and treatment center was required to accept all petitions and persons presented by county mental health professionals within its allotted area, whether or not such acceptance would overtax the institution's facilities. The problem of providing for creation and funding of adequate facilities was one for the legislature, the court said. —*Pierce County Office of Involuntary Commitment v. Western State Hospital*, 644 P. 2d 131 (Wash. Sup. Ct., April, 29, 1982).



# SOCIOS NUEVOS

## ACTIVOS

**D'Cruz, Oswald Albert, M.D.** - Escuela de Medicina de la Universidad de Navarra, 1970, Especialidad: Anestesiología - Ejerce en Mayagüez.

**De Sanctis Alsina, Vicente M., M.D.** - Escuela de Medicina de la Universidad Pedro Henríquez Ureña de Santo Domingo, 1975, Especialidad: Patología - Ejerce en Bayamón.

**Hernández Martínez, Pedro, M.D.** - Escuela de Medicina de la Universidad Santiago de Compostela en España, 1979, Especialidad: Medicina Interna.

**Muñiz Rodríguez, Manuel R. M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1978, Especialidad: Pediatría - Ejerce en Hato Rey.

**Nieves Torres, José A., M.D.** - Escuela de Medicina de la Universidad de Santiago de Compostela en España, 1975, Especialidad: Cirugía General - Ejerce en Mayagüez.

**Núñez Fernández, Luis R., M.D.** - Escuela de Medicina en la Universidad Javeriana de Bogotá, Colombia, 1967, Especialidad: Medicina Interna - Ejerce en Arecibo.

**Ocasio de Rosario, Hilda, M.D.** - Escuela de Medicina de la Universidad de Sevilla España, 1961, Especialidad: Medicina Interna-Neumología - Ejerce en Ponce.

**Ortega Prieto, Roberto, M.D.** - Escuela de Medicina de la Facultad Médica en Sevilla, España, 1972, Especialidad: Anestesiología - Ejerce en Mayagüez.

**Rodríguez González, Juan A.M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1973, Especialidad: Cardiología - Ejerce en Bayamón.

**Román Vélez, Angel M. M.D.** - Escuela de Medicina de la Universidad de Zaragoza en Madrid, España, 1973, Especialidad: Medicina de Emergencia - Ejerce en Arecibo.

**Román de Jesús, José C., M.D.** - Escuela de Medicina de la Universidad de Madrid, España, 1958, Especialidad Anestesiología - Ejerce en Mayagüez.

**Salazar García, Fernando, M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1974, Especialidad: Oftalmología - Ejerce en Mayagüez.

**Sánchez Rivera, Rafael, M.D.** - Escuela de Medicina de la Universidad Central de Madrid, España, 1960, Especialidad: Obstetricia y Ginecología - Ejerce en Bayamón.

**Santiago Pérez, María de los Angeles, M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1970, Especialidad: Pediatría - Ejerce en Patillas.

**Suárez Canabal, Dennis F., M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1976, Especialidad: Medicina Interna/Reumatología - Ejerce en Mayagüez.

**Torres Ortiz, Norman, M.D.** - Escuela de Medicina de la Universidad de Sevilla, España, 1973, Especialidad: Pediatría - Ejerce en Ponce.

**Torres Ortiz, Nydia E., M.D.** - Escuela de Medicina de la Universidad de Valencia, España, 1974, Ejerce en Bayamón.

## INTERNO - RESIDENTE

**Matías Valladares, Pedro F., M.D.** - Escuela de Medicina de la Universidad de Santiago de Compostela en España, 1981, Ejerce en Fajardo.

## ESTUDIANTE DE MEDICINA

**Chabrier Pérez, Mario** - Escuela de Medicina de la Universidad Autónoma de Santo Domingo. Se graduará en mayo de 1984.

## REINGRESOS

**Aguiló Zambrana, Juan, M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1960, Especialidad: Medicina Interna - Ejerce en Santurce.

**Badillo Borrás, Pedro, M.D.** - Escuela de Medicina de la Facultad de Medicina de Barcelona, España, 1973, Especialidad: Medicina General - Ejerce en Santurce.

**Bisbal, José E., M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1976, Especialidad: Medicina Física y Rehabilitación - Ejerce en Bayamón.

**Cruzado Pérez Enrique, M.D.** - Escuela de Medicina de la Universidad de Santiago de Compostela, España, 1974, Especialidad: Obstetricia y Ginecología - Ejerce en Hato Rey.

**Flores Martínez, José, M.D.** - Escuela de Medicina de la Universidad de Granada, España, 1960, Especialidad: Medicina General - Ejerce en Santurce.

**Huertas Rivera, Domingo, M.D.** - Escuela de Medicina de la Universidad de Cádiz - Sevilla, España, 1962 - Ejerce en Humacao.



**Irizarry Carmen G., M.D.** - Escuela de Medicina de la Universidad Central de Madrid - España, 1960, Especialidad: Anestesiología - Ejerce en San Juan.

**Lavergne, Rafael, M.D.** - Escuela de Medicina de la Universidad de Perú, 1954, Especialidad: Pediatría - Ejerce en Río Piedras.

**Márquez, Iván, M.D.** - Escuela de Medicina de Baylor, 1949, Especialidad: Cirugía - Ejerce en Santurce.

**Martí Nuñez, Rafael, M.D.** - Escuela de Medicina de la Universidad de Zaragoza, España, 1960, Especialidad: Medicina Interna - Ejerce en Caguas.

**Méndez Beauchamp, Víctor M., M.D.** - Escuela de Medicina de la Universidad Central de Madrid, 1962, Especialidad: Cardiología - Ejerce en Ponce.

**Méndez de Mercado, Asunción, M.D.** - Escuela de Medicina de la Universidad de Salamanca, España, 1971, Especialidad: Pediatría - Ejerce en Carolina.

**Quintero, Braulio, M.D.** - Escuela de Medicina de la Universidad de Cartagena, Colombia, 1972, Especialidad: Reumatología - Ejerce en Mayagüez.

**Ramírez De Arellano, S.R., M.D.** - Escuela de Medicina de la Universidad de Valladolid, España, 1958, Especialidad: Pediatría - Ejerce en Santurce.

**Riera Rodríguez, José D., M.D.** - Escuela de Medicina de la Universidad de Georgetown, Washington, D.C., 1962, Especialidad: Medicina Interna - Ejerce en Río Piedras.

**Rivera Paniagua, Dennis, M.D.** - Escuela de Medicina de la Universidad de Temple, 1951, Especialidad: Medicina Física y Rehabilitación - Ejerce en Guaynabo.

**Rodríguez Arroyo, Jesús M.D.** - Escuela de Medicina de la Universidad de Puerto Rico, 1972, Especialidad: Obstetricia y Ginecología - Ejerce en San Juan.

**Segarra Chaves, Carmen S., M.D.** - Escuela de Medicina de la Universidad de Creighton, Omaha, Nebraska, 1950, Especialidad: Obstetricia y Ginecología - Ejerce en Río Piedras.

**Varela, Gilberto E., M.D.** - Escuela de Medicina de la Universidad Central de Madrid, España, 1959, Especialidad: Medicina de Familia - Ejerce en Fort Benning, Georgia.

**Vázquez Oliveras, Humberto R., M.D.** - Escuela de Medicina de la Universidad de Salamanca, España, 1969, Especialidad: Pediatría - Ejerce en Santurce.

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## American College of Physicians

### ACP ISSUES RECOMMENDATIONS ON USE OF ARTHRITIS TESTS AND IMMUNOTHERAPY

The American College of Physicians (ACP) issued Clinical Efficacy Assessment Program (CEAP) recommendations on hyperbaric oxygen therapy for three conditions, automated ambulatory blood pressure monitoring, and various breath tests for diagnosing digestive disorders.

The College determined that the efficacy of *hyperbaric oxygen therapy in the treatment of acute, traumatic, peripheral ischemia* is not established; claims of efficacy rest on uncontrolled or anecdotal case reports.

Efficacy is also not established for *hyperbaric oxygen therapy in the treatment of chronic and acute peripheral vascular insufficiency*, the College declared. Although the therapy temporarily may relieve pain associated with chronic vascular insufficiency, the College points out that no data support its efficacy in stimulating the development of collateral circulation or in benefiting the course of the underlying disease.

Neither do controlled data support the use of *hyperbaric oxygen therapy in patients with venous ulcers*, according to the College. The ACP notes, however, that two small, uncontrolled series of case reports hyperbaric oxygen therapy as a possible adjunctive form of therapy in cases of self-limited, acute, peripheral arterial insufficiency due to drug toxicity, to permit time for the drug to be metabolized or excreted, or in cases of acute arteritis to provide time until other treatments can take effect.

*Hyperbaric oxygen therapy in the treatment of senility* also has not proved to be efficacious. The College calls for further research before making judgment as to the clinical usefulness of this therapy in the treatment of senility.

*Automated ambulatory blood pressure monitoring* may be a promising clinical research tool, but it lacks wide recognition as a proven and effective procedure in clinical medicine, the ACP has decided. The report notes that although the device is safe and can provide accurate 24-hour blood pressure measurements, drawbacks include the following: no studies have correlated the findings of 24-hour blood pressure monitoring with the natural history of hypertension and for long-term patient prognosis, and no advantage of the automatic device over repeated office measurements has been proved.

An automated ambulatory blood pressure monitoring device involves a cuff that automatically inflates at a given frequency. The device, which may incorporate data processing equipment, then measures blood pressure and records the results. The cost of a unit ranges between \$7,000 and \$22,000; the charge to the patient per study usually in \$130 to \$300.

*Breath tests for the diagnosis of various digestive disorders include  $^{13}\text{C}$  and  $\text{H}_2$  breath tests*, which are safe. Because  $^{14}\text{C}$  breath tests involve modest radiation exposure, the test benefits must be weighed against the radiation, exposure, especially in children and fertile women.

The  $^{13}\text{C}$  and  $^{14}\text{C}$  glycocholate tests may be clinically useful in diagnosing distal ileal dysfunction and the  $^{14}\text{C}$  xylose breath test is clinically useful for diagnosing bacterial overgrowth. Although the  $\text{H}_2$  breath test for diagnosing lactose intolerance appears to be highly accurate, diagnosis generally can be made by history alone—or by provocative exposure to lactose—containing products.

The  $^{13}\text{C}$  and  $^{14}\text{C}$  glycocholate and the  $\text{H}_2$  breath tests for diagnosing bacterial overgrowth, the  $^{13}\text{C}$ -trioctanoin and  $^{14}\text{C}$ -triolein breath tests for diagnosing malabsorption of fat, and the lactulose  $\text{H}_2$  breath tests presently do not warrant widespread clinical use.

Through the Clinical Efficacy Assessment Project, the ACP evaluates the effectiveness of nonsurgical medical tests, procedures and therapies and makes recommendations on their appropriate uses. To help physicians practice high quality, cost-effective medicine more efficiently, CEAP evaluations focus on the safety, efficacy and effectiveness of a clinical practice in internal medicine.

Dr. Schwartz, an assistant professor of medicine at the University of Pennsylvania School of Medicine, heads the three-year CEAP study, which is funded by a \$650,412 grant from The John A. Hartford Foundation. The private, New York City—located Foundation makes grants to stimulate health—care payment system reforms, to promote efficient energy use, and, through a fellowship program, to provide early career support for physicians in medical research. The Foundation, which has assets of \$135 million, granted \$7.7 million to projects in these three areas in 1980.



### PRIMATE MAY OFFER HANSEN'S DISEASE INSIGHTS

Louise, a mangabey monkey, may provide new insights into Hansen's disease, more commonly known as leprosy.

The African monkey came to the United States during the 1970s and was used in metabolism studies at the Delta Primate Research Center at Covington, Louisiana. In 1979 she developed skin lesions on her face, ears, and forearms which were identified as manifestations of Hansen's disease.

Because Louise's disease is typical of the human disease, the monkey offers investigators for the first time a practical model for study. The only animal model currently used is the nine-banded armadillo.

Interest in Hansen's disease has increased in the United States with the influx of refugees from South Asia.

The researchers believe tht Louise contracted the disease from her captors in Central Africa where thre are an estimated three million human cases. Her symptoms, however, did not appear for several years because of the long incubation period.

The researchers have started passage experiments between Louise and two other monkeys, Louis and Leonard. The investigators also hope to breed Louise to learn of genetic aspects of the disease.

### NEW USES INDICATED FOR BORON ANALOGS

Boron analogs, originally considered as possible cancer drugs, now show promise as a new and effective generation of drugs for the treatment of **rheumatoid arthritis**.

Boron analogs, so called because they can substitute the element of boron for carbon in certain amino acids, already have brought about many months of arthritis remission in rats that have a form of arthritis comparable to rheumatoid arthritis in humans.

Iris Hall, associate professor of the University of North Carolina School of Pharmacy, has tested the analogs for their effect upon prostaglandins, a family of chemicals in the human body that exert their effects on tissue locally and are known to have a variety of effects including the joint inflammation of rheumatoid arthritis.

Several antiprostaglandin drugs are now on the market for the treatment of rheumatoid arthritis. The boron analogs, however, have not shown any of the harmful side effects that some of these drugs exhibit and could open a new generation of drugs for such treatment. Further testing now is being conducted.

### NEW TECHNIQUE MAY OFFER CLUE FOR DIABETES STUDY

A complex new technique for singling out and identifying proteins has turned up a possible clue as to why some diabetics cannot handle sugar properly, even when they can produce insulin adequately.

Scientists from The Upjohn Company and Western Michigan University report that a unique protein resides in the cytosol of liver cells of spontaneously diabetic Chinese hamsters.

The variant protein may be an example of a cellular post-receptor defect characteristic of diabetes.

While the full import of the discovery is yet to be determined, the finding is one of the few instances of an apparent direct link between disease and a specific protein.

The variant protein found in the livers of the diabetic sublines of Chinese hamsters also is present in roughly constant quantity in hamsters before and after they have develo-

ped diabetes. Limited tests of livers from diabetic mice and humans have not demonstrated the variant protein, but further studies are planned.

"We would not be surprised to find it in other cells of diabetics", said Dr. David W. Sammons of Upjohn, "but perhaps not in the concentration noted in the highly active liver cells."

## aa AMERICAN ASSOCIATION BB OF BLOOD BANKS

### CDC REPORTS NEW AIDS CASES AABB RECOMMENDATIONS FORTHCOMING

The December 1982 issue of the Centers for Disease Control *Morbidity and Mortality Weekly Report* has revealed four new cases of Acquired Immune Deficiency Syndrome (AIDS) among hemophiliacs, bringing to seven the total number of hemophiliacs with AIDS which have been reported to CDC since July. The first case that provides a possible correlation with blood products other than plasma was also reported in the same publication. The patient is a 20-month old child who was transfused with blood products from 19 different sources during his first month of life. he subsequently developed unexplained cellular immunodeficiency and oportunistic infection. Investigation has revealed that one of the donors developed AIDS eight months after giving blood. The suspected blood product is platelets. The donor, a 48-year-old male, was in apparent good health when he donated blood but later became ill. he died in August of 1982.

A communication was sent to all Institutional and Associate Institutional Members on December 23 informing them of the new developments and expressing the Association's concern regarding AIDS and its relationship to the infusion of blood products. The AABB's Committee on Transfusion-Transmitted Diseases, chaired by Joseph Bove, MD, is assessing all available information and is in close communication with CDC, governmental agencies involved in investigating the AIDS problem, other blood collection agencies, and groups such as the National hemophilia Foundation.

The communication also reported that the suggestion had been made to treat hemophilia patients with single donor cryoprecipitate rather than AHF concentrate until the etiology of AIDS is firmly established. This may lead to an increase in the number of requests for cryoprecipitate.

Assistant Secretary of Health Edward Brandt, MD, convened a special conference on AIDS on January 4, attended by representatives of all concerned groups, including Dr. Bove for the AABB. The Transfusion Transmitted Diseases Committee then met in Washington, D.C., on January 6. Representatives from the American Red Cross, the Council of Community Blood Centers, and other concerned groups were also present. Consensus was reached at this meeting on seven recommendations, which will be mailed to the membership pending Board approval on January 11, 1983. The ARC and CCBC are expected to adopt the same or similar recommendations as the basis for handling the AIDS situation.





## American Academy of Family Physicians

The Board of Directors approved the composition and charge of the AAFP's new **Committee on Hospitals** at the Board's September-October sessions held in conjunction with the 1982 Annual Meeting in San Francisco. The new committee is an outgrowth of the Commission on Health Care Services.

Freshman Board member Robert McGinnis of Santa Barbara, Calif., was elected chairman of the new committee. In addition to the chairman, the committee will be composed of nine members representing the AAFP's nine regions.

The charge of the committee is "to study and develop recommendations on hospital privileges and inter- and intra-professional relationships in hospital. This committee will be responsible for providing members with information regarding hospital privileges, clinical departments, assisting members with hospital privilege problems to follow the designated protocol and making recommendations to the Board of Directors on policies or actions which the Academy may formulate or perform to improve hospital practice".

### COMMITTEE CHAIRMEN CHOSEN BY BOARD

Chairman of four other Academy committees were chosen at the Board meeting **Dr. Angel Mattos of Bayamon, Puerto Rico**, was re-elected Chairman of the Committee on Aging. he was elected chairman of the **Committee on Minority Health Affairs**.

Re-elected chairman of the Committee on Resident and Student Affairs was **Dr. Richard Inskip of Reno, Nev.** **Dr. Ernie Chaney of Beleville, Kan.**, the immediate past president, was elected chairman of the Publications Committee.

The Screening Committee is composed of AAFP President **Gerald Gehringer of New Orleans** (who serves as chairman); Board Chairman **Robert Higgins of Bremerton, Wash.**; President elect **Harmon Holverson of Emmett, Idaho**; and **Dr. Chaney**. Directors appointed to the committee are **Dr. Jeanne Arnold of Hanover, N.H.**; **Dr. Robert Taylor of Spartanburg, S.C.**, and **Dr. McGinnis**.

### COST EFFECTIVENESS

The Board endorsed continuation of a project study the cost effectiveness of health care delivered by family physicians. The Academy will work with **Dr. Alvin R. Tarlov of Chicago** in developing cost effectiveness protocol to be incorporated into the National Outcome Study, which is funded in part by the Robert Wood Johnson Foundation.

**Dr. Tarlov**, Professor of Medicine at the University of Chicago Department of Medicine, is the principal investigator of the study.

In an effort to provide a continuing avenue for communication, the Board approved Academy participation in a liaison committee to be composed of two representative each from the AAFP, the American Academy of Pediatrics and the American College of Physicians. **Dr. McGinnis** was appointed to represent the Board, and **Claudene Clinton**, director of the Academy's research and Information Resources Division, was appointed to represent the staff.

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## PHYSICIANS SPEAK OUT ON BRAIN INJURY IN BOXING

In the Jan. 14, 1983 issue of the *Journal of the American Medical Association*, the AMA is reiterating its stand taken in 1982 recommending improvements in medical standards for boxing that could make the sport safer.

The AMA is calling for the establishment of a computerized national boxing registry to record the results of all licensed bouts, including information on injuries sustained by individual boxers. Medical representative of state and local boxing commissions could use these data to set standards for the physical examination of boxers, develop measures to prevent brain injury and determine criteria for discontinuing a bout for medical reasons.

The registry is one of a series of practical safeguards recommended for boxing by the AMA's Council on Scientific Affairs. The council does not recommend banning the sport completely, which it views as an unrealistic way of coping with the problem.

The ring physician, according to the council, should be authorized to stop any bout at any time to examine a boxer or to end the fight. Medical evaluations should be standardized, the council says, and one way to do this is to urge state and local commissions to conduct medical training seminars for all ring personnel.

The use of plastic safety mats and padded cornerposts has already improved the safety of the sport, and the council encourages the continued development of such equipment.

Although the AMA believes boxing to be no more dangerous under supervised conditions than many other contact sports, it recognizes that the usual cause of deaths in boxing occur from brain injury and recommends that bouts be permitted only where adequate brain surgery facilities are immediately available.

The recent death of Korean boxer Duk Koo Kim has drawn an outcry against the brutality of boxing from many individual physicians, whose thoughts are reflected in additional contributions in this *JAMA*.

Although he acknowledges the AMA report to be "solid, balanced, and reasonable," *JAMA* editor George D. Lundberg, MD, takes issue with its position that boxing should be better controlled rather than banned altogether. No caring person can enjoy a sport, he suggests, that has the principal aim of rendering one's opponent injured, defenseless, incapa-

citated and unconscious. "Boxing is wrong at its base," Lundberg contends, and "as a throwback to uncivilized man, should not be sanctioned by any civilized society."

In a second editorial Maurice W. Van Allen, MD, from the University of Iowa Hospitals and Clinics, Iowa City, calls boxing "a fragment of our savagery" that should be ignored by the mass media and left "to those who enjoy privately staged dogfights." Neither Van Allen nor Lundberg accepts the commonly advanced arguments that boxing allows disadvantaged youths a chance at fame and financial opportunity or that boxing provides a legal outlet for man's innate aggressiveness. There may be some surface truth to those notions, these writers say, but at what price in injury and degradation to successful and unsuccessful boxers alike?

Adding to the body of knowledge associating boxing with brain injury, Ronald J. Ross, MD, and colleagues from Radiologic Medical Imaging Associates, Mayfield Heights, Ohio, report on their study of 40 ex-boxers who suffered symptoms including headaches, visual and speech disturbances, loss of memory, and muscular coordination and locomotion problems.

Ross took a boxing history from each man and examined all except two with computed tomographic (CT) scans. More than half of the men also underwent neurologic testing and electroencephalography (EEG). The CT scans were used to detect enlargement of the natural fissures and cavities of the brain caused by atrophy of brain tissue.

Ross found that EEG abnormalities and the presence and severity of brain atrophy correlated strongly with the number of bouts each boxer had fought. "The significance of our data is particularly striking," Ross writes, "in view of the fact that we actually had few professional fighters who had numerous bouts."

Brain atrophy showing up on CT scans would reflect damage that occurred at least months and probably years before, according to Ross. Because of their usefulness in detecting brain injury, Ross recommends that CT scans and EEG examinations be considered part of regular neurological examinations for active boxers.

## RAPE TRAUMA SYNDROME

Perhaps one of six women in this country will become a victim of rape, which has been called the nation's most rapidly increasing violent crime. The way rape victims are treated by physicians and hospital personnel, police officers, and their families and friends can greatly influence their recovery from the experience.

Rape victims commonly suffer a stress disorder called rape trauma syndrome. A description of the symptoms and a call for greater sensitivity to the psychological needs of rape victims appears in the Jan. 28, 1983 issue of *JAMA* in a special communication to physicians by Catherine A. Martin, MD, and G. Richard Braen, MD, from the University of Kentucky College of Medicine, and Mary Cabel Warfield, MA, MS, from the Lexington Rape Crisis Center, Lexington, Kentucky.

Immediately after being raped, some women may display a wide range of emotions openly, while others may mask their feelings and appear composed or subdued. "A victim's out-



ward behavior may not reflect the degree or nature of the emotional crisis she is experiencing", the authors warn.

After being raped, a woman may feel tired, have tension headaches, startle easily and suffer sleep disturbances, particularly if she was awakened from sleep by the assault. She may also complain of decreased appetite, food not tasting right, nausea when thinking of the assault and abdominal pain.

Recovery from rape can be slow, the authors say. The woman may have chronic vaginal irritation, changes in menstruation, depression and nightmares. She may develop fears and phobias evoked by situations symbolic of the rape, such as a man whose appearance resembles the rapist's.

The most frequently encountered complication of rape, the authors explain, is an aversion to sexual activity, usually developing gradually over a period of months. Women in whom aversion does not develop may still find less pleasure in sexual intimacy or may experience pain during intercourse and difficulty in achieving orgasm.

Rape victims often find it difficult to regain a feeling of safety. Many women stay at home or go out only with friends. Some may move or change their telephone numbers.

Friends and relatives of rape victims may feel supportive but have little idea of how to help. They may mistakenly expect a fast recovery or encourage a survivor not to talk about the assault. If a woman is unable to talk to relatives or friends, the authors advise, she should seek support from a knowledgeable clergyman, a rape crisis service or a professional counselor.

Relatives and friends, hospital personnel, police officers and juries find it easier to believe and support a rape victim if she has physical injuries and if the assailant was a stranger. They tend to express more doubt and give less support to a victim who has no visible injuries or who was raped by someone she knew. "Despite the recent shift away from thinking of rape as a sexual experience to realizing that it is a violent assault, there is still a tendency to see the victim as responsible", the authors report. They advise physicians to warn rape victims of the possibility of these negative reactions.

### HEPATITIS B VACCINE: KNOWN SAFETY AND UNKNOWN RISKS

Two federal Food and Drug Administration (FDA) physicians writing in the Feb. 11, 1983 *Journal of the American Medical Association* underscore the safety of the newly licensed hepatitis B vaccine and urge that vaccination of high risk groups continue.

The statement by Robert J. Gerety, MD, and Edward Tabor, MD, comes in the wake of concern that some blood plasma used in making the vaccine is obtained from hepatitis B-positive male homosexuals, who have been the most numerous victims, so far, of acquired immune deficiency syndrome (AIDS). There has been speculation that AIDS may be caused by an agent that can be transmitted through blood or blood products.

According to Gerety and Tabor, however, "the known risk of hepatitis B for persons in high-risk groups [hospital workers, homosexuals, intravenous drug abusers] far exceeds the risks of vaccine-induced infection by a theoretical transmissible agent that would have to survive the purification and

inactivation procedures applied to the licensed hepatitis B vaccine."

The manufacturing processes to which Gerety and Tabor refer, which include treatment of the donated blood plasma with pepsin, urea and formaldehyde, have been designed to inactivate all known groups of animal viruses by interfering with their ability to reproduce and infect human cells.

Only one known case of Kaposi's sarcoma, a tumor characteristic of AIDS, has developed among the more than 19,000 persons who were vaccinated in several clinical trials of the vaccine, according to Cladd Stevens, MD, of the New York Blood Center, New York City, who is quoted in a "Medical News" section article in the Feb. 11 *JAMA*. Eleven cases of AIDS have since occurred among 3,600 male homosexuals who remained unvaccinated in a Blood Center trial, while the case of Kaposi's sarcoma occurred among the 1,083 men who were vaccinated.

Subsequent to another clinical trial run by the Centers for Disease Control (CDC), Atlanta, more than 30 cases of AIDS have occurred among 5,986 unvaccinated men, while no cases have appeared among 714 vaccinated men, says Donald Francis, MD, from the CDC branch in Phoenix.

Because the frequency of AIDS among vaccine recipients in the trials is lower so far than that reported in nonvaccinated participants, there has been some speculation that the hepatitis B vaccine may protect against AIDS. But, Francis objects, "We have no evidence for that right now, although it appears that [the vaccine] is not causing the disease."

### ESTROGEN REPLACEMENT IN THE MENOPAUSE

Despite the known benefits of estrogen replacement therapy in the menopause, physicians and patients alike are concerned that its use may be associated with uterine cancer. In an assessment of research findings, the American Medical Association calls the hazard of estrogen—induced uterine cancer "relatively remote" but recommends that physicians base their treatment of each patient on an individualized weighing of benefits and risks.

AMA guidelines for the use of estrogen in menopause, adopted in 1982 in an AMA Council on Scientific Affairs report, appear in the *Journal of the American Medical Association*.

Estrogen replacement therapy has proved useful in controlling the "hot flashes" associated with the menopause and in relieving the irritation and painful intercourse that can result from atrophy of vaginal tissue. Estrogen therapy has been most effective in arresting or retarding osteoporosis that increases the risk of fractures in postmenopausal women.

Recent evidence also suggests that estrogen replacement may protect against atherosclerotic heart disease and heart attacks, the AMA report adds.

Research analyzed for the report suggests that women treated with estrogen daily for two to four years have up to eight times the risk of developing uterine cancer as untreated women. The risk seems to decline after therapy is discontinued, however, and no increase in the death rate from uterine cancer has been noted, possibly because tumors in estrogen-treated women seem to be less "aggressive". In fact, the risk of death is less than that attributed to smoking one pack of cigarettes a day, the report says.

Other unwelcome side effects of estrogen replacement therapy include abnormal uterine bleeding, fluid retention, breast enlargement and growth of preexisting benign uterine tumors ("fibroids").

"As with any form of drug therapy, estrogens should be used only for responsive indications, in the smallest effective dose and for the shortest period that satisfies therapeutic need." In addition, physicians are warned to monitor the cumulative dosage of estrogen ointments and creams applied to vaginal tissues and to examine at least annually women treated with estrogen, even though they may not complain of symptoms.

### CAUTION IN TREATING MILD HYPERTENSION URGED

Most American physicians routinely prescribe drug therapy for patients with mild hypertension—those whose diastolic blood pressure ranges between 90 and 104 mm Hg. In a Jan. issue of *JAMA*, however, three physicians question the validity of the research on which this practice is based and suggest that most of these patients are unlikely to have less cardiovascular disease or live longer because of the medication.

Mild hypertension affects about 30 million people in the United States. They make up about 75 percent of all hypertensives and about 15 percent of the population. The impetus to treat this group, according to Norman M. Kaplan, MD, University of Texas Health Science Center, Dallas, grew out of six studies conducted in the 1960s and 1970s, particularly the Hypertension Detection and Follow-Up Program (HDFP), which found that mortality could be reduced by almost 20 percent with medication. But defects in the design of these studies cast serious doubts on the validity of their findings, Kaplan says.

In addition, Kaplan points out, the results of the Multiple Risk Factor Intervention Trial (MRFIT), recently published in *JAMA* [September 24, 1982], suggest that treatment for mild hypertension does not reduce the risk of death and may actually harm some patients.

Research findings that show a substantial *percentage* improvement in illness and death rates associated with treatment for mild hypertension tend to overshadow what may be a very small increase in *actual* numbers of individual patients who are helped, according to Thomas G. Pickering, MD, from the New York Hospital-Cornell University Medical Center. The basic question is this: "Should we subject large numbers of persons to long-term treatment with potentially harmful medications when the chances of any one person deriving benefit from the treatment are small?"

Probably not, says Neil Harding McAlister, MD, from the Toronto General Hospital. Antihypertensive medications have troublesome side effects—male impotence, for example. Feeling condemned to take drugs for the rest of one's life for what seems to be an "incurable" disease can be psychologically debilitating. "Until definitive advice is forthcoming, close observation of mild hypertensives seems a reasonable course of action," McAlister concludes.

Patients should be encouraged to follow nondrug therapies that are likely to help, such as weight reduction for the obese, moderate sodium restriction and relaxation techniques, Kaplan adds. Those at relatively high risk for cardiovascular disease for reasons other than blood pressure, however, may

benefit from drug therapy, both Kaplan and Pickering agree, although these patients are more likely to be protected against strokes than heart attacks, according to Pickering.

"Some patients with mild hypertension who've had unpleasant side effects from their blood pressure medication may take heart from these reports," says Richard J. Jones, MD, director of the AMA's Division of Scientific Analysis and Technology. "Drug therapy for mild hypertension, particularly for patients under 50, may indeed have been overrated. However, because patients may be at risk for cardiovascular disease and stroke for reasons other than blood pressure, no patient should discontinue his medication without discussing all the risk factors with his physician."

### AMA CALLS FOR REDUCING DIETARY SODIUM

Calling for control of dietary sodium not only for people with high blood pressure and those at risk for developing high blood pressure, but also for the general public, the AMA published in a February 11, 1983 issue of the *Journal of the American Medical Association* its report on sodium in processed foods.

The AMA report, the result of a study by its Council on Scientific Affairs and an AMA-sponsored conference on sodium labeling held last year, puts the Association strongly in support of food industry initiatives to list sodium content on packaged foods. The medical community's principal concerns are that reliable information about the sodium content of packaged foods be available to patients whose daily sodium intake must be limited and that a wide range of sodium-labeled foods be available to allow variety in these patient's diets.

While the degree to which sodium intake influences the development of high blood pressure is not known, it is accepted medical practice to prescribe antihypertensive medication and weight loss when indicated and to consider moderate dietary sodium restriction.

The AMA report notes that nearly 40 million adults in this country have either high blood pressure or borderline high pressure. High blood pressure is the major risk factor for strokes and one of the major risk factors in heart disease. High blood pressure is known to increase the risk for congestive heart failure and kidney failure as well.

The sodium labeling program of the Food and Drug Administration (FDA) receives AMA support in the report. Along with encouraging overall reduction of sodium in processed foods and calling for voluntary food industry sodium labeling standards, the FDA will participate in public education programs explaining the relationship of sodium and high blood pressure and using label information on sodium. Food industries and their trade associations are also engaged in public education efforts, as are the AMA and a number of other professional associations.

Other recommendations in the AMA report include calls for physicians to counsel their patients about restricting dietary sodium and for food industries to include information about potassium content in their voluntary labeling programs.

According to the AMA, "all segments of the population need the best combined educational efforts of the health professionals, government and industry" about sodium in proces-



sed foods and about the relationship of sodium consumption to the potential development or control of high blood pressure.

### ALCOHOL FOUND TO RAISE LEVELS OF "GOOD" CHOLESTEROL IN INACTIVE MEN

A group of Houston researchers reports in the *Journal of the American Medical Association* of February 11, 1983 that drinking a controlled amount of ethyl alcohol each day raises the level of high-sensitivity lipoprotein cholesterol (HDL) in the blood of inactive men. Increased levels of HDL have been associated statistically with a decreased risk of coronary heart disease.

A team led by G. Harley Hartung, PhD, from the Baylor College of Medicine, studied 16 marathon runners, 15 joggers and 13 men who did not regularly exercise, all between the ages of 27 and 59 years. None of the men had a history of coronary heart disease or were taking any medications that would affect the level of HDL in their blood. Routine alcohol consumption was similar in each of the three groups.

During the study, each of the men abstained from drinking alcohol for a period of three weeks and then drank alcoholic beverages equivalent to three 12-ounce cans of beer daily for a second period of three weeks. Blood levels of HDL were measured at the start of the study and the end of each period.

Hartung's group found that the joggers and the inactive men had about the same levels of HDL at the beginning of the study, while HDL levels in the runners were higher. Among the inactive men, abstinence from alcohol resulted in a substantial drop in HDL levels, which rose again to previous levels when drinking was resumed. Neither abstinence nor drinking, however, had any effect on HDL levels among the runners or joggers.

Although the authors admit that these findings might fuel an impulse to believe that regular consumption of alcohol can protect against heart disease, they don't encourage that interpretation. "It is not known whether increasing HDL level reduces the risk of coronary heart disease," they point out. Moreover, a large body of medical literature "links the excessive consumption of alcohol with adverse physiological and social conditions, including cirrhosis of the liver, hypertension, cardiomyopathy, pancreatitis, and a host of social problems related to alcoholism."

### VIDEO GAMES HAZARDOUS TO PATIENTS WITH LIGHT-SENSITIVE EPILEPSY

Video games can be hazardous to people with light-sensitive epilepsy, caution neurologists from the Mayo Clinic in a Feb 1983 issue of *JAMA*.

The physicians report the case —the first documented in the United States— of a 15-year-old boy with no previous history of epilepsy who suffered seizures while playing Pac-Man, a popular video game.

"Later, the boy had three more generalized seizures, always associated with bright, early morning sunlight," write Neil R. Dahlquist, MD, James F. Mellinger, MD, and Donald W. Klass, MD. The case is similar to two reports from England last year.

"We consider seizures induced by playing video games

similar to television-induced seizures, which have been well-recognized in epileptic patients who are sensitive to flickering lights or geometric patterns," the authors say.

The boy was treated with valproic acid, a drug effective in patients with light-sensitive epilepsy and he suffered no recurrence of seizures.

He also quit playing video games.

### INJURIES, NOT OVERDOSE, NOW LEADING CAUSE OF "LUDES" DEATHS

Deaths associated with use of the drug methaqualone are on the upswing, and injury has replaced overdose as the leading cause of these fatalities, according to Charles V. Wetli, MD, Deputy Chief Medical Examiner, Dade County, Florida.

In a Feb. issue of *JAMA*, Wetli reports findings from his study of 246 deaths related to abuse of methaqualone hydrochloride, popularly known as "ludes" [from the trade name Quaalude], occurring in the Miami metropolitan area between January 1971 and December 1981. Twenty-eight percent of the deaths occurred in 1981 alone, and more than 75 percent occurred since 1977.

Methaqualone was once widely prescribed as a sedative. Its reputation for inducing euphoria and having aphrodisiac qualities had made it a popular recreational drug of abuse.

In Wetli's study, 70 percent of the victims were white males, and 26 percent were white females. Their average age was about 25 years. Less than five percent of the victims were black, although blacks make up 17 percent of the population of Dade County.

Drug overdose accounted for 68 deaths (28 percent) of which 40 were judged accidental and 28 suicidal. Three deaths (one percent) involved disease in which methaqualone abuse was judged incidental. The remaining 175 deaths (71 percent) were due to injuries sustained in motor vehicle and other accidents (106 cases), and in homicides (31 cases).

Sixty-two percent of the overdose deaths occurred before 1978, but 93 percent of the accidents occurred since 1977.

Three-quarters of the accidents involved motor vehicles. Many of the drivers, passengers and pedestrians were found to have alcohol and other drugs in addition to methaqualone in their blood. The drivers reportedly lost consciousness at the wheel, speeded, or failed to make necessary driving maneuvers.

"The effect of methaqualone, alone or in combination with other substances, is most reminiscent of that of acute alcoholic intoxication," Wetli says, leading to poor judgement, impulsive actions, lack of motor coordination and sleepiness.

Large quantities of illicit methaqualone, often adulterated with other drugs, are smuggled into this country from South America, according to Wetli. Adding to the street supply of the drug, he says, are sham "stress" clinics that provide prescriptions for methaqualone with little or no legitimate medical justification.

The rapidly increasing incidence of methaqualone — related motor vehicle accidents is a significant threat to the public. Wetli calls on physicians to avoid prescribing methaqualone when reasonable alternatives exist, for stronger legislation to restrict the distribution of methaqualone as well as to provide for detection of the drug in apparently intoxicated motorists and for curbs on the importation of illicit methaqualone.

# ASOCIACION MEDICA DE PUERTO RICO

# BOLETIN

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuercen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

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El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquina a doble espacio; por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

### Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

### Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

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Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigos) y el autor. Debe indicarse en la parte superior de la ilustración.

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Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

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Las referencias deben ser numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

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*Villavicencio R: Soplos Inocentes en Pediatría, Bol. Asoc. Med. P. Rico 1981; 73(10): 479-87*

Si hay más de 5 autores, incluir los primeros 3 y añadir et al.

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Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquina a doble espacio, no deben ser mayor de 500 palabras, ni incluir más de cinco referencias.

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All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

### Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

### Nomenclature

Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially).

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These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

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Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

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An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

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### Letters to the Editor

Will be published at the discretion of the Editorial Board. They should be typewritten double-spaced, should not exceed 500 words nor more than five references.



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San Juan , 7 al 10 de abril de 1983.

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Con sumo placer queremos anunciar que los días 7, 8, 9 y 10 de abril de 1983, se celebrará en el Hotel Condado Holiday Inn el Primer Congreso Puertorriqueño de Cardiología.

A esta actividad científica, auspiciada por todas las Sociedades de Cardiología del país, y por la Escuela de Medicina de la Universidad de Puerto Rico, se darán cita distinguidos invitados de fama internacional y cardiólogos locales para discutir los más recientes adelantos en el diagnóstico y manejo de las enfermedades cardiovasculares de adultos y niños.

Entre los temas a discutirse se han seleccionado los de más relevancia en la práctica diaria, como: Enfermedad Coronaria, Muerte Súbita, Hipertensión Arterial, Marcapasos, Arritmias y Agentes Antiarrítmicos, Farmacoterapia Cardiovascular, Enfermedades Valvulares, Fallo Cardíaco, Enfermedades Congénitas, y otras enfermedades con que comúnmente se confronta el médico en su práctica diaria.

Este evento científico ha sido diseñado de tal manera para que sea de utilidad para Cardiólogos, Internistas, Cirujanos Cardiovasculares, Médicos de Familia y Generalistas.

Gracias a los patrocinadores, esta actividad educativa se ofrecerá a un precio módico para que se beneficie el mayor número de médicos de la comunidad. Los asistentes al curso recibirán 20 horas crédito en Categoría I.

Próximamente recibirán más información sobre esta histórica actividad, esperamos reserven la fecha en su calendario.

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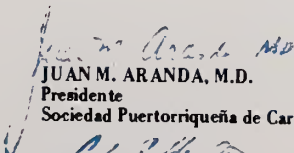
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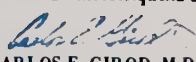
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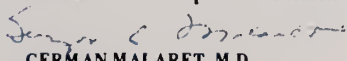
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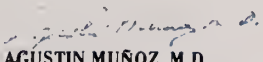
  
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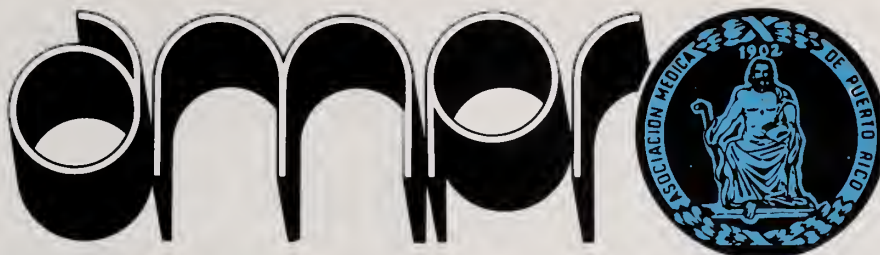
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# Columna del Editor



Este número de abril reviste gran significado para nuestra Asociación, ya que en él se le rinde tributo al ilustre médico puertorriqueño Don Agustín Martínez de Andino.

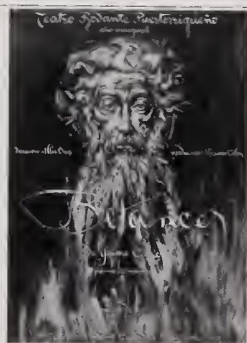
Los que tuvimos el privilegio de trabajar bajo su tutela podemos dar fe de sus conocimientos médicos y la seriedad y dedicación con que ejercía su profesión. El gran amor y respeto que hacia ella sentía lo exigía a diario de aquel grupo que para el 1965 daba sus primeros pasos en el ejercicio de la medicina. Su devoción a la medicina y a la patria quedará siempre de manifiesto en nuestro recuerdo de ese gran hombre.

Es por ello que nos llena de satisfacción el poder ver como sus discípulos y sus compañeros le dedican hoy el fruto de su trabajo. La Asociación Médica de Puerto Rico, y la Junta Editora del Boletín, se sienten honrados con la decisión de la Sociedad Puertorriqueña de Endocrinología y Diabetología de utilizar nuestro órgano oficial para plasmar este tributo científico a la memoria de uno de nuestros más prominentes miembros.

Rafael Villavicencio, M.D.  
Presidente Junta Editora  
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Marzo 1983

ASOCIACION MEDICA DE PUERTO RICO

**BOLETIN**



VOL 75/NUM 4

ABRIL 1983

## NUESTRA PORTADA

Una vez más honra la portada de nuestro Boletín una obra del insigne maestro puertorriqueño Lorenzo Homar. Este cartel reproducido fotomecánicamente de una pintura original en acrílico de Homar, fue comisionado por la directora del "Puerto Rico Traveling Theater", Myriam Colón, para el estreno mundial de una obra de Jaime Carrero en la ciudad de Nueva York. El mismo no ha sido reproducido en ninguna otra forma y es visto y divulgado por primera vez en Puerto Rico a través de nuestro Boletín. El texto, dibujado directamente sobre la pintura original, fue realizado por el maestro Homar basándose en la caligrafía del propio Betances.

Varias razones nos indujeron a seleccionar esta obra para nuestra portada de este mes. El Dr. Agustín Martínez de Andino, a quien dedicamos esta edición, fue un entrañable amigo del artista. Juto a un pequeño núcleo de amigos de Lorenzo, respaldó asiduamente al taller del maestro Homar. Agustín Martínez de Andino fue además el fundador de La Casa Nacional de la Cultura y un serio coleccionista de pintura y gráfica local y universal. Fue asimismo un agudo observador clínico y un dedicado profesional, y su rectitud y amor por Puerto Rico fueron siempre ejemplares. Bien podemos decir que el Dr. Martínez de Andino fue un médico en la tradición de Betances, y al celebrarse este mes el natalicio de aquel prócer, nada más apropiado que honrar su memoria con esta portada.

B.J. Marqués, M.D.

# EDITORIAL



Al salir a la publicación este número que dedica la Sociedad Puertorriqueña de Endocrinología y Diabetología en tributo a la memoria del Dr. Agustín Martínez de Andino nos embarga un gran dolor por la pérdida de nuestro querido Manolo. El Dr. Manuel E. Paniagua fue el primer endocrinólogo en llegar a Puerto Rico y fue el autor de los primeros estudios clínicos en Endocrinología y Diabetes publicados por un endocrinólogo puertorriqueño en el Boletín de la Asociación Médica de Puerto Rico y en revistas nacionales. Fue un internista cabal y en dicha capacidad dirigió los departamentos de Medicina Interna del Hospital de Distrito de Arecibo (1945-46) y el Hospital Municipal de Río Piedras (1950-1965).

Colaboró con el Dr. Gregory Pincus, en el estudio pionero del uso de los contraceptivos para el control de la fertilidad en Puerto Rico. Cuando el Dr. Agustín Martínez de Andino se unió a la facultad de la Escuela de Medicina en el anterior Hospital Municipal de San Juan, se hicieron grandes amigos y juntos colaboraron en varios estudios clínicos. Ambos desarrollaron la Sección de Endocrinología del Hospital Municipal de San Juan, Rafael López Nussa, sección que dirigió en el período desde 1973 a 1980. Fue miembro fundador de nuestra Sociedad y juntos Agustín y Manolo proveyeron el liderato, la motivación, y el entusiasmo necesario para el desarrollo de la misma.

La publicación de este número no hubiese sido posible sin la cooperación y determinación de Manolo.

Es el autor principal de uno de los trabajos científicos que se publican en este número y en otros dos el co-autor. Fue ironía del destino que no vivió para verlo publicado.

Con el deceso de ambos, ha perdido Puerto Rico dos bastiones de la Medicina.

La matrícula de la Sociedad les vivirá eternamente agradecida por sus sabias enseñanzas, su ejemplo y su estímulo.

Lillian Haddock Suárez, MD  
Presidenta, Sociedad Puertorriqueña  
de Endocrinología y Diabetología





**Dr. Agustín Martínez de Andino**

## IN MEMORIAM

El 18 de octubre de 1981, la Sociedad Puertorriqueña de Endocrinología y Diabetología ofreció en su convención anual la primera conferencia en tributo a la memoria del Dr. Agustín Martínez de Andino, uno de los miembros fundadores de la Sociedad, médico y científico ejemplar quien honró con sus ejecutorias nuestra profesión. Fue el Dr. Agustín Martínez de Andino uno de los pioneros en el desarrollo de la Endocrinología y Diabetología en Puerto Rico, en la enseñanza de dichas disciplinas en la Escuela de Medicina de la Universidad de Puerto Rico, y en la práctica de la especialidad para beneficio de la comunidad puertorriqueña.

Obtuvo el grado de bachillerato en Ciencias, con una concentración en Química de la Universidad de Puerto Rico en 1941. Cursó sus estudios de Medicina y su educación postgrado en Medicina Interna y Endocrinología y Diabetes en el "Jefferson Medical College" de Philadelphia. A su regreso a Puerto Rico estableció su práctica privada y se unió a la facultad clínica de la Escuela de Medicina, cuando apenas estaba esta comenzando la enseñanza clínica a su primera clase graduanda en el Hospital Municipal de San Juan.

Dirigió el servicio de Endocrinología y Diabetes de dicho hospital desde el 1952 al 1968 y dirigió la sección de Endocrinología y Diabetes del Departamento de Medicina de la Escuela de Medicina desde el 1952 al 1959, cuando esta transfirió su taller clínico al Hospital Universitario. Comenzó el primer programa de adiestramiento postgrado en Endocrinología y Diabetes en la Escuela de Medicina en el año 1957 y continuó desarrollando dicho programa en el Hospital Municipal de San Juan.

Fue miembro de múltiples organizaciones profesionales; la Asociación Médica de Puerto Rico, la Sociedad de Endocrinología Americana (Endocrine Society), la Asociación de

Diabetes Americana (American Diabetes Association), el Colegio Americano de Médicos (American College of Physicians), la sociedad honoraria Alpha Omega Alpha y otras.

A su muerte había publicado artículos en su especialidad y subespecialidad. Es co-autor de un artículo que se publica en este número y varios no publicados aún.

Su labor cívica fue extensa y dedicada. Fue miembro del Ateneo Puertorriqueño y Presidente y fundador de la Casa Nacional de la Cultura; miembro del Instituto Puertorriqueño de Cultura Hispánica, miembro de la Junta de Directores de la Asociación pro Museo Histórico de Puerto Rico, presidente del Club Rotario de Isla Verde, y miembro de la Junta Ejecutiva, "Boy Scouts of America".

Trabajó arduamente como presidente de campaña para la recaudación de fondos para la construcción de la escuela e iglesia de Nuestra Señora de la Piedad en Isla Verde.

Fue un amante del arte, la música y sobre todo la Medicina.

Además de ser un extraordinario profesional y maestro fue un devoto esposo y padre.

El pueblo de Puerto Rico, la Asociación Médica de Puerto Rico y la Universidad de Puerto Rico se honró con tan insigne profesional. El siempre vivirá en el recuerdo de su familia, sus amigos, sus alumnos y compañeros en la profesión.

**Lillian Haddock Suárez, M.D.**  
Presidenta, Sociedad Puertorriqueña  
de Endocrinología y Diabetología





# The labyrinth of the lung

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The labyrinth of the lung...  
a sculptural representation  
of the microscopic terminal  
airways, respiratory bronchioles  
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Please see following page for brief summary of prescribing information, including warnings, precautions, and adverse reactions.



# The labyrinth of the lung

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15 mg/ml (approx. 0.65 mg delivered with each metered dose)
  - Alupent Metered Dose Inhaler is prescribed more often than any other inhaler<sup>1</sup>
- Alupent Syrup 10 mg/5 ml**
  - It tastes as good as it tests

† When administered by IPPB.

<sup>1</sup> Pharmaceutical Data Services, Phoenix, Arizona.

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**Contraindications:** Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated.

**Warnings:** Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent, brand of metaproterenol sulfate, as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in several cases.

Paradoxical bronchoconstriction with repeated excessive administration has been reported with other sympathomimetic agents. Therefore, it is possible that this phenomenon could occur with Alupent, brand of metaproterenol sulfate.

Patients should be advised to contact their physician in the event that they do not respond to their usual dose of a sympathomimetic amine aerosol.

**Precautions:** Because Alupent, brand of metaproterenol sulfate, is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympathomimetic amines.

**Information for Patients:** Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

**Carcinogenesis:** Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed.

**Pregnancy:** Teratogenic Effects: Pregnancy Category C. Alupent, brand of metaproterenol sulfate, has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose and 62 times the human oral dose; the teratogenic effects included skeletal abnormalities and hydrocephalus with bone separation. Oral reproduction studies in mice, rats and rabbits showed

#### Syrup Tablets Metered Dose Inhaler Inhalant Solution

no teratogenic or embryocidal effect at 50 mg/kg, or 310 times the human inhalation dose and 31 times the human oral dose. There are no adequate and well-controlled studies in pregnant women. Alupent, brand of metaproterenol sulfate, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Alupent, brand of metaproterenol sulfate, is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness of Alupent Metered Dose Inhaler and Inhalant Solution in children below the age of 12 have not been established. The safety and efficacy of Alupent Tablets in children below the age of 6 have not been established.

**Adverse Reactions:** Adverse reactions are similar to those noted with other sympathomimetic agents.

The most frequent adverse reactions to Alupent, brand of metaproterenol sulfate, are nervousness, tachycardia, tremor and nausea. Less frequent adverse reactions are hypertension, palpitations, vomiting and bad taste.

**Overdosage:** The symptoms of overdosage are those of excessive beta adrenergic stimulation listed under **Adverse Reactions**. These reactions usually do not require treatment other than reduction of dosage and/or frequency of administration.

**How Supplied:** Round, white, scored tablets of 10 and 20 mg in bottles of 100. Metered Dose Inhaler containing 225 mg of metaproterenol sulfate (300 inhalations); 15 mg per ml (approximately 0.65 mg delivered with each metered dose). Cherry-flavored syrup, 10 mg per teaspoonful (5 ml), in 16 oz bottles. Inhalant Solution 5% in bottles of 10 ml with accompanying calibrated dropper.

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# AGRADECIMIENTO

La utilización de papel cromado de alta calidad para la publicación de este número del Boletín de la Asociación Médica de Puerto Rico ha sido posible gracias a una donación de la Cooperativa de Ahorro y Crédito de la Asociación Médica.

La Junta Editora del Boletín de la Asociación Médica de Puerto Rico le da las gracias por este medio a todos los miembros de la Cooperativa, en especial a su Junta de Directores con cuya aportación hemos podido lograr la excelencia gráfica que nuestro órgano oficial se merece.

# ESTUDIOS CLINICOS

## The Clinical, Biochemical, Operative and Pathological Analysis of 38 Cases with Primary Hyperparathyroidism

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**Summary:** Thirty eight subjects with primary hyperparathyroidism were diagnosed and operated in the University Hospital in the period from 1960 to 1975. Twenty eight were females, ten males and the age range was from sixteen to seventy. The predominant symptoms were referable to the gastrointestinal and urinary systems. Sixty one percent had nephrolithiasis and seven patients had peptic ulcer disease. In seven patients the diagnosis was suspected when hypercalcemia was found in routine chemistries. Bone disease was present in thirteen cases. Hypercalcemia and hypercalciuria were the most consistent laboratory findings. The serum alkaline phosphatase was elevated in eleven subjects and the urinary hydroxyproline in ten. There was a strong positive correlation between both parameters. Only one of the subjects who had both parameters elevated was reported to have no bony lesions suggestive of hyperparathyroidism in the skeletal survey.

Thirty one of the subjects had parathyroid adenomata, twenty nine single and two multiple. Five had chief cell hyperplasia and two had carcinoma. Seventy seven percent of the tumors were located in relation to the right and left lower pole of the thyroid. The two patients with carcinoma have had a very benign course.

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*Presented in the 1975 Annual meeting of the Puerto Rico Medical Association. Supported by Research Training Grant TI-AM-5097 from the National Institute of Arthritis and Metabolic Diseases, U.S.P.H.S. and Grant FR-0063 from the Division of Research Facilities and Resources, U.S.P.H.S.*

Since the advent of automatization, with the routine determination of serum calcium, the diagnosis of primary hyperparathyroidism is being made more frequently. While in the past the diagnosis was suspected if the patient had bone disease, recurrent renal lithiasis or intractable peptic ulcer disease, today the diagnosis is made at a time when the patient in many occasions is asymptomatic. The increased frequency in which this disease is diagnosed nowadays has shown that this endocrine disorder is not uncommon. The prevalence of hyperparathyroidism may be as high as one case per 1,000 of the adult population.<sup>1</sup>

This same trend has been reflected in the diagnosis of hyperparathyroidism in the University Hospital.

It is the purpose of this publication to document our experience in the diagnosis and management of 38 cases with primary hyperparathyroidism diagnosed in the University Hospital from 1960 to 1975.

### Materials and Methods

The subjects were studied in the Clinical Research Center and the medical wards of the University Hospital. Laboratory studies included: serum calcium, phosphorus, alkaline phosphatase, uric acid, electrolytes and other routine serum chemistries; the levels of calcium, phosphorus and urinary hydroxyproline were measured in repeated 24 hr. urine collections. Other special studies included, phosphate and creatinine clearance, and percentage tubular reabsorption of Phosphorus. Radioimmunoassay for PTH was performed in a selected case as a courtesy of the PTH Immunoassay Laboratory of the Massachusetts General Hospital.

In every subject a bone survey, an intravenous pyelogram and an upper gastrointestinal series was performed. In some subjects slit lamp examinations and X-rays of the lamina dura were performed.

The sources which led to the diagnosis of hyperparathyroidism in these 38 subjects included: screening program in subjects with renal lithiasis and peptic ulcer disease, in four patients hypercalcemia was found in the course of the evaluation of thyroid nodular mass, one of the cases was diagnosed by histopathological examination after being admitted to the hospital directly from the Tumor Clinic for removal of what was thought to be a thyroid nodule and in the remaining an elevated serum calcium was found in a routine SMA 12.



## Results

## Clinical Data

Table I summarizes the composition of the series. A total of 38 subjects were operated; 28 females and 10 males. The youngest patient was 16 and the oldest 73. While 18 cases were diagnosed in a period of 10 years (1960-69) in the subsequent five years, with the introduction of SMA 12 screening, 20 cases were diagnosed.

TABLE I

**Primary Hyperparathyroidism  
University Hospital (1960-75)**

1. Total Number of Cases .....	38
2. Sex Distribution	
Male .....	10
Female .....	28
3. Youngest patient (years) .....	16
4. Oldest patient (years) .....	73
5. Year Distribution	
1960 .....	3
1961 .....	2
1962 .....	3
1963 .....	1
1964 .....	1
1965 .....	2
1966 .....	1
1967 .....	0
1968 .....	1
1969 .....	4
1970 .....	1
1971 .....	1
1972 .....	5
1973 .....	4
1974 .....	6
1975 .....	3

TABLE II

**Primary Hyperparathyroidism  
(UDH: 1960-75)**

**Prominent Symptoms and Signs in 38 Cases**

1. Weakness .....	11
2. Headaches .....	11
3. Weight loss .....	9
4. Bonyaches .....	11
5. Neuropsychiatric .....	4
6. Gastrointestinal	
a. Nausea & vomiting .....	3
b. Epigastric pain and discomfort .....	16
(not associated with PUD)	
c. Constipation .....	11
7. Urinary Symptoms	
a. Referable to renal lithiasis .....	20
b. Polydipsia and polyuria .....	5
(not assoc. with renal lithiasis)	

TABLE III

**Primary Hyperparathyroidism  
(UDH: 1960-75)**

**Prominent Physical Findings in 38 Cases**

1. Band Keratopathy .....	1
2. Palpable adenoma .....	4
3. Nodular Thyroid .....	5
4. BP greater than 140/90 .....	10
5. Bone tenderness .....	3
6. Calcific deposits in skin .....	1

Tables II and III show the prominent clinical features. The predominant symptoms were those referable to the gastrointestinal, the urinary and the neuromuscular systems.

The most common gastrointestinal complaints were epigastric pain and discomfort which in seven cases was associated with radiologically proven peptic ulcer disease. Constipation was the next most common symptom. One patient had acute pancreatitis.

The most common urinary symptoms were those referable to renal lithiasis, as renal colic, recurrent urinary tract infection and hematuria. Polydipsia and polyuria associated with the hypercalcemia and without the presence of renal

lithiasis was seen in five subjects. Muscle weakness was a prominent clinical findings.

Physical findings were not diagnostic of the disease in any instance. In one subject band keratopathy was diagnosed by slit lamp examination, four had a palpable nodule in the neck at the site where the tumor was found later on and five had a nodular thyroid mass. In ten subjects at some time a blood pressure greater than 140/90 was found, three had diffuse bony tenderness and one had calcification on the skin.

Table IV summarizes the modes of presentation of the 38 cases. The most common mode of presentation was symptomatology referable to renal lithiasis. Of interest are the cases that were discovered by chance (serendipity).

TABLE IV

Modes of Presentation in 38 Cases of Primary Hyperparathyroidism University Hospital (1960-76)	
Renal Lithiasis .....	17
Nephrocalcinosis, Brown Tumor and Pathological Fracture .....	1
Renal Insufficiency .....	1
Peptic Ulcer Disease .....	4
Thyroid Mass .....	4
Serendipity (SMA <sub>12</sub> ) .....	7
MEA Family .....	1
Diabetes Insipidus .....	1
Klinefelter (SMA <sub>12</sub> ) .....	1
M. I., Pancreatitis .....	1

Table V summarizes the incidence of nephrolithiasis and renal disease in the 38 cases. Twenty-three of the patients had renal lithiasis (61%). Bilateral involvement was present in 13, two had nephrocalcinosis, nine had unilateral renal calculi and the remaining one had a bladder calculi. Prior to the

TABLE V

Nephrolithiasis and Renal Disease in 38 Cases with Primary Hyperparathyroidism	
1. Number of Cases with Lithiasis .....	23
2. Percentage of total .....	61%
3. Duration of Symptoms (Renal colic and passage of renal calculi) .....	hours to 18 years
4. Anatomical Distribution	
a. Unilateral Renal Calculi .....	9
Right .....	4
Left .....	5
b. Bilateral .....	13
c. Nephrocalcinosis .....	2
d. Bladder calculi .....	1
5. Operative procedures prior to Diagnosis	
a. Right nephrectomy .....	2
b. Left nephrectomy .....	2
c. Ureterolithotomy .....	5
6. Cases with Renal Insufficiency	
Improved Renal Function .....	3
Unchanged .....	1
Death .....	1

diagnosis of primary hyperparathyroidism, nine had undergone some operative procedures for their renal lithiasis. Five had ureterolithotomy, two had undergone right nephrectomy and another two a left nephrectomy. In three of five patients, renal insufficiency was present. The post-operative renal function improved in three.

Table VI summarizes the main clinical features presented by the patients who had peptic ulcer disease.

Of the seven patients with peptic ulcer disease, in four the main symptoms were those referable to peptic ulcer disease and in the remaining three the main symptoms were all those pertaining to chronic renal lithiasis. Of the latter, two had a nephrectomy performed and a third had undergone a partial nephrectomy. In all the subjects with peptic ulcer disease the ulcer was located in the duodenum, in one the clinical course was complicated by gastrointestinal bleeding, in two by obstruction and in one of these two perforation occurred. Only one of these patients has had recurrence of his ulcer symptomatology nine years after removal of the parathyroid tumor. The remaining subjects have remained asymptomatic after removal of the tumor. Three of these patients had mild demineralization of the osseous structure.

TABLE VI

Primary Hyperparathyroidism University Hospital 1960-75							
Patient	Date of operation	Onset of Ulcer Symptoms	Main Sex of Hyperpara.	Localization of ulcer	Complications of ulcer disease	Operation	Follow-up
J.H.F.	9/1/60	Age 55 Proven by U.G.I. Series	Referred to peptic ulcer disease	Duodenal	Obstruction Perforation	Duodenorrhaphy	No further complaints post op. Death M.I. 1972
J.S.F.	9/21/61	Age 42 Proven by U.G.I. Series	Renal lithiasis Rt. partial nephrectomy-1955 Peptic ulcer sxs.	Duodenal 1961-active crater at base of duod. cap.	None	None	Asymptomatic Hx epidermoid Ca of tongue
J.A.R.	9/10/64	Age 59 Proven by U.G.I. Series	Polyuria, polydipsia. Sxs referable to P.U.D.	Duodenal 1968-active crater	Persistent pain, partial obstruction	None	Recurrence of pain
F.V.S.	10/9/73	Age 38 Dx. duod. ulcer at U.S.A.	Sxs referable to P.U.D. Sxs referable to lithiasis on the past	U.G.S. 9/66, D.U. 1967 def. duod. bulb.	Upper G.I. Bleeding 1963	None	Asymptomatic
V.A.D.	11/5/72	Age 59 Eggs, pain Age 68 UGIS, D.U.	Sxs referable to P.U.D.	1971 ulcer crater duod. apex, 1972 def. duod. bulb.	None	None	No definite ulcer sxs.
C.N.C.	1/30/69	Age 61 proven by UGI series	Renal lithiasis Lt. nephrectomy 64	1966 def. duod. bulb & antrum 1968: D.U.	None	None	Asymptomatic
M.B.V.	5/18/71	Age 56 U.G.I.B.	1 Renal lithiasis Rt. nephrectomy 2 Chronic U.T.I. 3 Creat. cl. 2.4 mg/min.	1969 - ulcer crater duod. bulb 1970 - hiatal hernia	None	None	No ulcer sxs.

### Radiological Findings

Thirteen of the subjects showed radiological evidence of bone disease. In four this was characterized by diffuse demineralization with sub-periosteal resorption. Osteoporosis was a prominent radiologic finding in nine. Two of these subjects had compression fractures of the vertebrae. The other had a brown tumor in the right ischium and a pathological fracture of the right pubic bone.



Table VII summarizes the results of the bone roentgenological examination.

TABLE VII

**Bone Disease in 38 Cases of  
Primary Hyperparathyroidism  
(U.D.H. 1960-75)**

Diffuse demineralization with ..... Subperiosteal Resorption	4
Osteoporosis.....	6
Compression Fracture, ..... Osteoporosis	2
Brown Tumor of Rt Ischium,..... Fracture Pubic Bone, Osteoporosis	1
<b>TOTAL.....</b>	<b>13</b>

Of these 13 subjects four had bone disease only, six had bone disease and renal lithiasis, two had bone disease and hypercalcemic nephropathy, and one had bone disease and peptic ulcer disease.

### Laboratory Findings

Figures one to four summarize the laboratory findings. Figure I shows the serum calcium range in 37 subjects. The dotted circle represents the mean, the triangle the upper value and the open circle the lower value. The mean represents the average of anywhere from six to 15 determinations. All were hypercalcemic but at some time seven of the subjects had normal serum calcium levels.

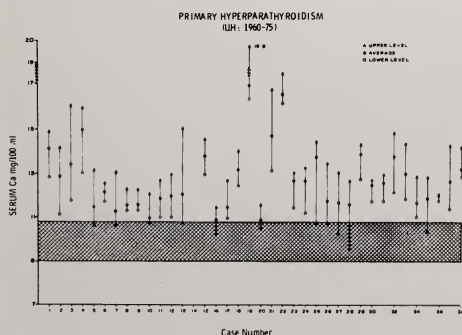


Figure 1: Serum calcium levels in 37 subjects with primary hyperparathyroidism.

Figure II shows the serum phosphorus range in the same subjects. Twenty seven had low average values but nine of these had normal serum phosphorus value in some instances. Ten subjects had normal average values although seven had low serum phosphorus at some time. Of the latter group of patients three had renal disease.

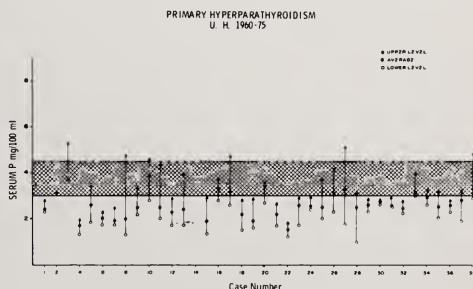


Figure 2: Serum phosphorus levels in 37 subjects with primary hyperparathyroidism.

Of the two subjects which always had normal serum phosphorus; one had severe renal disease and the other one had serum phosphorus at the lower limits of normal.

The urine calcium was elevated at some time in most of the subjects (Figure III). Five subjects had values within normal limits (#37, 33, 27, 24, 13). Of these five, two had renal disease with impaired creatinine clearance, one was on IV fluids and the intake of calcium was low when the laboratory examinations were performed and the remaining two had normal renal function.

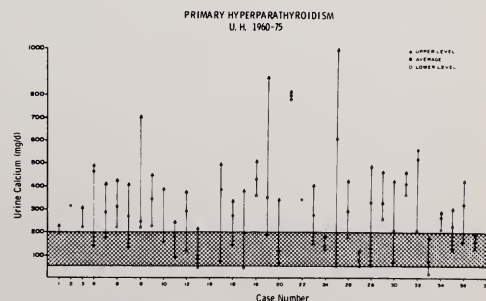


Figure 3: The 24 hr urinary calcium levels in 37 subjects with primary hyperparathyroidism.

### Phosphate clearance vs. Tubular Reabsorption of Phosphate

The phosphate clearance and the percentage TRP were determined in 21 subjects. All had normal creatinine clearances and hypophosphatemia. In sixteen of these 21 subjects these parameters were abnormal (normal phosphate clearance > 10ml/min, normal percentage TRP > 86%).

## Urinary hydroxyproline and Alkaline Phosphatase

The serum alkaline phosphatase was determined in all the subjects and was elevated in 11. The 24 hr. urinary hydroxyproline was determined in 20 subjects and was found elevated in 10 (Figure IV). In eight of these 10, the alkaline

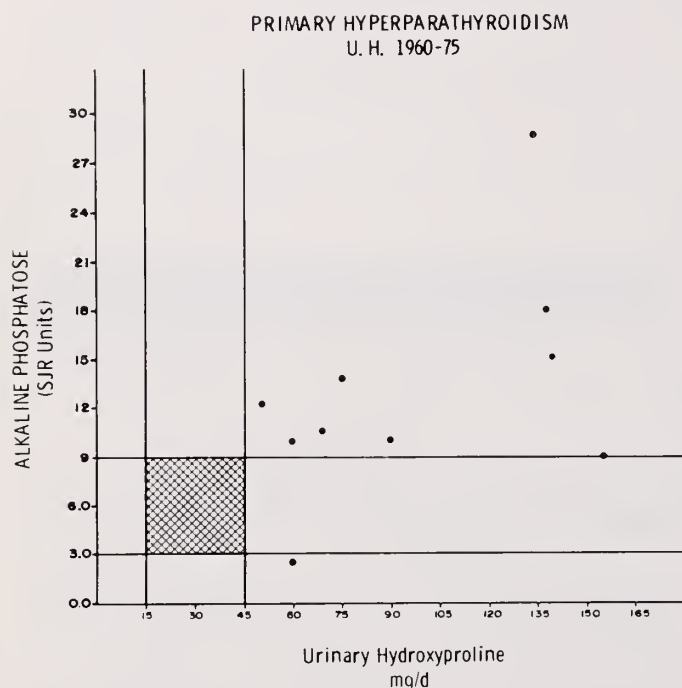


Figure 4: The 24 hr urinary hydroxyproline correlation with the serum alkaline phosphatase in ten subjects with primary hyperparathyroidism.

phosphatase was also elevated. There was a strong positive correlation between both parameters ( $r = 0.69$ ). Only one of the subjects who had both parameters elevated was reported to have no bone lesions suggestive of hyperparathyroidism in the skeletal survey.

### Other Laboratory Studies

The serum uric acid was performed in 23 subjects and was elevated in nine females and two males.

### Pathological Data

Table VIII summarizes the location of the tumor and the pathology. Twenty nine of the lesions were single adenoma and two had multiple adenomata (79.9%), five had hyperplasia (14.2%) and two had carcinoma. Seventy seven percent (77%) were located in relation to the lower poles of the thyroid, two were located within the thyroid (one of these a carcinoma) and one was located in the mediastinum.

The weight of these adenomas ranged from a microscopic size to 113 gms. Twenty-eight were chief cell adenoma, two were mixed chief cell and clear cell adenoma, and one was a mixed chief and oxyphil cell adenoma.

Five had chief cell hyperplasia and two had parathyroid carcinoma.

Several of the tumors had areas of cystic degeneration. In one of the patients with carcinoma with cystic degeneration

TABLE VIII

Pathology and Location of Parathyroid lesions (U.D.H. 1960-75)		
	No. of Cases	Percentage
Parathyroid adenoma	31	79.9%
Single	29	
Multiple	2	
Hyperplasia		14.2%
Chief cell	5	
Parathyroid CA	2	5.9%
Location		
RLP; LLP	24	77%
RUP; LUP	4	
Thyroid	2	
Mediastinum	1	

the immunoreactive PTH was measured in the plasma and in the cystic fluid. The plasma level was 100 ul eq/ml and the level in the cystic fluid was 37 ng/ml (upper limit of normal are 15ul eq/n and 0.8 ng/ml respectively).

### Post-Operative Complications

Five subjects had hypocalcemia post operatively. The serum calcium ranged from 6.7 to 7.8 mg/dl. This hypocalcemia was transient and lasted from one to six weeks. In these five subjects the serum phosphorus increase during the period of tetany ranged from 1.6 mg/dl to 3.3 mg/dl (in a subject it rose from 1.8 to 3.4, in another subject it rose from 2.1 to 5.4 mg/dl).

One subject developed a local hematoma in the neck and one developed superior laryngeal paralysis.

One patient remained hypercalcemic after the removal of one parathyroid adenoma and a second has had intermittently elevated calcium levels after removal of only three glands rather than 3 1/2 for treatment of hyperplasia.

### Discussion

The use of multichannel biochemical screening of large populations undergoing medical examinations has revealed a considerably higher incidence of primary hyperparathyroidism than had previously been recognized. Boonstra and Jackson<sup>1</sup> described 50 cases of proven hyperparathyroidism diagnosed from 50,000 routine serum calcium analysis, an incidence of at least one case per 1,000 in their hospital. Purnell<sup>2</sup> in the Mayo Clinic found an incidence of 1.4% in the routine clinical examinations of 1,630 patients who were relatively asymptomatic.



Williamson<sup>3</sup> in the screening of 4,727 adult hospital inpatients found an incidence of one case per 945.

Hyperparathyroidism occurs two to three times more frequently in the adult female population. In a review of 322 cases Norris<sup>4</sup> published a ratio of 3 to 1. Among 350 cases diagnosed by Watson,<sup>5</sup> 243 or 70% were female. Out of 171 proven cases of hyperparathyroidism, Purnell<sup>1</sup> encountered 56 males and 115 females, a ratio of 2 to 1. Our experience compares with that of other authors for 74% of our cases were females.

The spectrum of manifestations in primary hyperparathyroidism has evolved significantly since Mandl<sup>5</sup> performed the first parathyroidectomy in a patient with cystic bone disease.

In the mid thirties Albright<sup>6</sup> noted the frequent existence of kidney stones in hyperparathyroidism. Subsequently other associated conditions were recognized such as: psychosomatic disorders,<sup>7</sup> peptic ulcer disease<sup>8</sup> pancreatitis,<sup>9</sup> and its association with multiple endocrine adenomata.<sup>10</sup> Randall,<sup>11</sup> Keating<sup>12</sup> and Purnell<sup>1</sup> have emphasized the presence of chemical hyperparathyroidism in patients without clinical manifestations which has led to the hypothesis that the majority of patients with primary hyperparathyroidism may have asymptomatic disease which is non progressive and may be followed with periodic observation rather than immediate surgical removal.

Our series illustrates all the protean clinical manifestations that can be seen in hyperparathyroidism.

Calculus disease of the urinary tract still remains the most common clinical manifestation in hyperparathyroidism. The incidence of primary hyperparathyroidism may vary from two to as high as ten percent in various stone clinics.<sup>13</sup> On the other hand the incidence of renal lithiasis in primary hyperparathyroidism may vary from 50 to 90 percent.<sup>13 14 15 16 17 18</sup> An incidence of 61% in our series compares to that reported in the literature. Nephrocalcinosis is not a frequent complication and was seen in two of our cases. Gonder<sup>19</sup> has reported that 46 of a series of 100 cases required urologic surgery before their disease was diagnosed. Nine of our 23 cases with calculus disease of the urinary tract required renal surgery prior to the diagnosis. Of interest is a case referred with the diagnosis of diabetes insipidus because of marked polydipsia and polyuria caused by the hypercalcemia. Hypercalcemia induced by injections of parathyroid extract results in depression of the glomerular filtration rate and marked disturbance in renal concentrating mechanism.<sup>20</sup> The latter is explained on basis of a decreased ability of the cells lining the loops of Henle and the collecting duct of pumping sodium out of the tubular urine and into the medullary interstitium<sup>21</sup> and by an alteration of the permeability of the collecting duct to water in the presence of a hypercalcemic state.<sup>22</sup> This has also been shown in other hypercalcemic states. Of the five subjects with renal insufficiency two had hypercalcemic nephropathy not associated with gross radiological evidence of nephrolithiasis.

Gastrointestinal symptoms are the second most frequent set of symptoms seen in patients with primary hyperparathyroidism. These were first noted by Gutman<sup>23</sup> in 1934. Rogers<sup>24</sup> in 1946 suggested that peptic ulcer disease was aggravated by this disorder. Ostrow<sup>25</sup> in 1960 made a review of several large series and reported an incidence of peptic ulcer disease varying from seven to 25 percent. A composite analysis of these series gave an over-all incidence of peptic ulcer disease in primary hyperparathyroidism of 9.1 percent. In our small number of cases seven out of 38 had peptic ulcer disease, an incidence of 18 percent, higher than that encountered in most

series but similar to the incidence in Howard's<sup>26</sup> and Hellstrom's series.<sup>27</sup> When conversely a series of patients with peptic ulcer disease is screened for primary hyperparathyroidism the incidence has varied from one to three percent.<sup>28</sup> In our small series three out of 128 subjects with peptic ulcer disease were diagnosed as having primary hyperparathyroidism, an incidence of 2.3 percent which compares to that reported in the literature.

The studies of Donnegan<sup>29</sup> have shown that single parathyroid hormone injections without an accompanying hypercalcemia consistently cause gastric hypersecretion. These authors have likewise shown that an abrupt rise in serum calcium independent of parathyroid hormone consistently increase the production of pepsin, gastric secretory volume and free acid either in normal or in hypoparathyroid subject. The gastric response to prolonged hypercalcemia in man has not been systematically studied. The fact that all patients do not demonstrate basal hypersecretion suggest that an adaptation to the hypercalcemic state may occur. Thus, further investigation on the effect of hyperparathyroidism and hypercalcemia on gastric function is warranted. About 40 to 50 percent of patients with hyperparathyroidism and peptic ulcer disease heal their ulcers postparathyroidectomy. The remarkable improvement and healing in our seven cases with peptic ulcer disease are witness to this effect.

One of our cases had an acute pancreatitis. It has been estimated that hyperparathyroidism may be the cause of pancreatitis in about seven percent of cases.<sup>30</sup> The pathophysiologic basis of this association may be related to one of two mechanisms. First, parathyroid hormone, in experimental animals has been shown to cause hemorrhagic pancreatitis but there is no evidence to suggest that this occurs in man.<sup>31</sup> Second, inspissation of calcium phosphate salts within pancreatic ductular structures may lead to ductal obstruction and pancreatitis. However, intraductal calculi and obstruction occur in the absence of pancreatitis and viceversa, so the correlation is not a close one.

While in the 1930's and 40's the diagnosis of primary hyperparathyroidism was made when skeletal changes occurred, the condition is now usually diagnosed and treated long before the skeletal changes can be recognized radiologically. Histologically, bone biopsy of all cases of primary hyperparathyroidism shows evidence of bone disease.<sup>32</sup> The parameters used clinically to detect bone disease such as roentgenologically skeletal survey, serum alkaline phosphatase and urinary hydroxyproline are not sensitive enough to detect bone disease in the early cases of primary hyperparathyroidism. In our series thirteen (34%) cases had bone disease radiologically evident. In five of these patients the bone disease was diagnostic of hyperparathyroidism. Four showed generalized demineralization of the bones and subperiosteal resorption and one had a brown tumor of the right ischium and a pathological fracture of the pubic bone besides generalized demineralization.

Of these 13 cases urinary hydroxyproline was determined in 11 and was found to be elevated in ten. Only eight of the ten that had had urinary hydroxyproline elevated had hyperphosphatasia. A strong positive correlation was demonstrated between both parameters.

A technique being used today to detect early osteopenia is that of radiographic densitometry of selected osseous structures.<sup>33 34</sup> This technique is not being routinely used as yet.

Regarding the biochemical diagnosis of primary hyper-

parathyroidism we agree with the contention of all other investigators in the field that an elevated serum calcium is the best diagnostic parameter provided all other causes of hypercalcemia are ruled out.

McGeown<sup>35,36</sup> was the first to comment on the spontaneous fluctuations in serum calcium that sometimes occurred in hyperparathyroidism and noticed occasional normal values could be seen. Connor<sup>37</sup> in his series of 32 cases demonstrated an incidence of 12.5 percent of what he called intermittent hyperparathyroidism. Such fluctuations were also found in seven of our cases. For that reason whenever we suspect hyperparathyroidism we like to perform repeated serum calcium determinations and we do not rule out the disease on basis of only one laboratory determination.

Normocalcemia<sup>38,39</sup> has been encountered in proven cases of hyperparathyroidism. When we encounter normocalcemia in a suspect we follow them closely with repeated serum calcium determinations. In all instances we have observed wide fluctuations of the serum calcium and hypercalcemia.

Serum phosphate and other tests of phosphate metabolism such as phosphate clearance, and percentage tubular reabsorption of phosphate have been found to be within normal limits in about 50 percent of the cases with primary hyperparathyroidism.<sup>40</sup>

The serum level of phosphorus will depend upon the duration and severity of the disease. In the analysis of our 38 cases we can say that except for two cases all our subjects were hypophosphatemic at sometime. One of these two cases had renal disease and in the other the serum phosphorus was in the lower limit of normal.

Parathormone is known to promote the tubular reabsorption of calcium. The hypercalciuria of hyperparathyroidism occurs because of the elevated serum calcium and increased clearance not compensated by the parathyroid hormone effect on the renal tubules. In early and mild cases of hyperparathyroidism, hypercalciuria may not be encountered. Excluding the patients which had azotemia, only two of our patients had normocalciuria, an incidence of 5%. Strott<sup>41</sup> has reported an incidence of 24% normocalciuria in his series and Mallette<sup>42</sup> an incidence of 46%.

With the development of the radioimmunoassay of parathormone a formidable tool has been added to the group of tests used for the diagnosis of hyperparathyroidism. In early assays performed by Berson and Yallow<sup>43</sup> they failed to show elevated levels in 13 out of 28 cases with proven hyperparathyroidism. In more sensitive and precise assays Arnaud<sup>44</sup> and Reiss<sup>45</sup> have shown elevated levels in 95% and 100% respectively of the cases.

The surgeon routinely identifies all the glands and proceeds to remove the adenoma or adenomata. In the case of hyperplasia 3 1/2 glands are removed. Four of our cases with hyperplasia have been cured of the disease. In the remaining case only three glands were removed. Primary hyperparathyroidism may be caused usually by adenomas of the parathyroids which may be single or multiple, and less commonly by primary hyperplasia and carcinoma of the gland. Adenomas are usually found in the neck (90 percent) but in 10 percent of the cases they may be found in aberrant positions such as the anterior mediastinum and in the substance of the thyroid. Most of the tumors are located inferior to or near the lower poles of the thyroid.<sup>46</sup>

Only in one of our cases was the tumor found in the mediastinum, the tumor being the second largest (113gm) in

the literature.

To have a parathyroid carcinoma in two of our 38 cases is rather unusual. Although parathyroid carcinomas are rare it should be suspected when hyperparathyroidism is accompanied by a palpable tumor in the neck, specially in the male and with serum calcium concentration over 14 mg/dl.<sup>47</sup> The pathologic criteria for its diagnosis include mitosis, dense fibrous strands surrounding the original adenoma, vascular invasion and lymphatic or visceral metastasis.<sup>48,49</sup> Histologically the parathyroid tissue differs very little from that of a benign tumor. Our cases show three of the criteria for malignancy. There is not as yet evidence of local or visceral metastasis and the serum calcium has remained normal, in both 16 and 12 years respectively after the operation. The interval between operation and recurrence varies from three months to nine years with a median value of two years.<sup>50</sup>

The finding of a parathyroid adenoma in what was thought to be a thyroid nodule is not novel, for this has been recorded in many instances in the literature. The association of thyroid disease in 40 percent of patients with primary hyperparathyroidism,<sup>51</sup> and viceversa warrants that a serum calcium be done routinely in all patients with thyroid disease. The thyroid lesions present in patients with primary hyperparathyroidism include benign nodular lesions, carcinoma, and chronic lymphocytic thyroiditis.

The finding of a parathyroid adenoma imbedded in the thyroid is not unusual. In our series one adenoma and one carcinoma were found in the thyroid tissue.

The types I and II multiple endocrine adenomata was not encountered in any of our cases. One of the patients was found to have a microscopic papillary adenocarcinoma of the thyroid and one of the subjects was the member of a family studied in the VA Hospital with a multiple endocrine adenomata syndrome.

**Resumen:** Se presenta una serie de treinta y ocho casos de hiperparatiroidismo primario diagnosticados en el Hospital Universitario en el período de 1960 a 1975. Veintiocho sujetos pertenecen al sexo femenino y diez al sexo masculino. Los síntomas predominantes presentados fueron referentes al sistema gastrointestinal y urinario. Sesenta y un por ciento de los sujetos tenían nefrolitiasis y siete padecían de úlcera péptica. En siete se diagnosticó la condición al encontrarse hipercalcemia en un análisis químico de rutina. Trece sujetos tenían enfermedad osea. Los hallazgos de laboratorios más consistentes fueron hipercalcemia e hipercalciuria. La fosfatasa alcalina sérica estaba elevada en once pacientes y la hidroxiprolina urinaria en diez. Se demostró una fuerte correlación positiva entre ambos parametros. Solamente a un sujeto que tenía ambos parametros elevados se le diagnosticó no tener enfermedad osea por radiografía.

Treinta y uno de los sujetos tenían adenomas paratiroides, veintinueve solitario y dos múltiples. Setenta y siete por ciento de los tumores se encontraron localizados en relación a los polos inferiores de los lóbulos tiroideos. Los dos pacientes con carcinoma han presentado un curso benigno.



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# Incidence of Hypothyroidism After Radioiodine Treatment for Graves Disease

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**Abstract:** During the 16 years period of 1965-1981 one hundred seventy-three (173) patients with hyperthyroidism, all but 4 with Grave's disease, were treated with  $^{131}\text{I}$  at the San Juan City Hospital. Forty-eight (28%) were lost to follow-up and 52 (41.6% of the remaining 125) required more than one dose. The other 73 treated with an average dose of 3.47 mCi (3-5 mCi) were followed up for from 1-12 years (total of 275 patient-years). Thirteen of them (18%) became hypothyroid within one year of treatment and the cumulative percentage rose gradually at an average rate of 3.2% per year up to 38% in 12 years. These figures are higher than those obtained in similar series of low dose radioiodine therapy. If this tendency is confirmed by other studies it would point towards a higher sensitivity to the effects of  $^{131}\text{I}$  among the Puertorrican population.

The treatment of hyperthyroidism, especially its most common form of Grave's disease, has been highly unsatisfactory and probably will remain so until its etiology is unraveled and a more specific therapy may be devised. Both surgery and radioactive iodine are only ablative treatment (although the latter is certainly less risky) and the antithyroid drugs are little more than symptomatic therapy used until the disease goes into "spontaneous" remission. Unfortunately, there is a very high percentage of recurrence after medical treatment varying between 25 and 50% in different series, and many patients are quite impatient with such prolonged therapy.

With the advent of radioiodine we thought an answer had been found to the surgeon's dilemma: too radical a thyroidectomy will result in a higher percentage of hypothyroids while the opposite technique would not "cure" enough patients. Since the administration of radioiodine is such a simple procedure, we decided to use much smaller doses than were being used in other institutions<sup>1,2,3</sup>, risking a low percentage of one-dose "cures" to obtain the lowest possible incidence of hypothyroidism, and using repeated doses whenever necessary.

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We have been aware of the fact that upon prolonged periods of observation similar percentages of hypothyroidism occur after surgery and radioiodine.<sup>4</sup> Indeed, it may occur after drug therapy or no therapy at all. Still, if hypothyroidism is inevitable, we believe in postponing it as long as possible. Contrary to the "practical" school of thought whose adepts believe in using large doses of radioiodine, deliberately inducing hypothyroidism and giving immediate replacement therapy, we are averse to the idea of curing a disease by inducing another, although a much more manageable one. Needless to say, we have always tried to individualize our patients and this has been done by the procedure described below.

## Materials and Methods

All patients considered by their physicians as candidates for radioiodine therapy were screened by a Radioiodine Therapy Board consisting of two or more specialists in Nuclear Medicine, one or two surgeons and the entire Section of Endocrinology of the Department of Medicine of the San Juan City Hospital. Most patients came from the Endocrinology Clinic of the San Juan City Hospital but 8-10% came from the private practices of the attending physicians. Each patient was evaluated as to type and duration of the disease, age, complications, response to previous treatment and other pertinent factors.

Of the 173 patients treated during the 16-year period covered by this report (1965-1980), three had multinodular goiters and one had a toxic adenoma. The remaining 169 had Graves' disease, in two of them recurring after surgery and in one appearing 10 years after hypophysectomy for chromophobe adenoma followed by panhypopituitarism on substitution therapy. There were 22 (13%) males, which is the usual percentage for Graves' disease.

The dose recommended varied with the size of the gland and its avidity for iodine as determined by previous  $^{131}\text{I}$  uptake. No attempt was made to "guesstimate" the weight in grams but each gland was classified as small (up to twice normal size), medium (two to four times normal) or large (over four times normal). The dose given varied between two and five mCi with a mean of 3.47 mCi.

## Results

As shown in Table 1, of the original 173 patients, 48 (28%) were lost to follow-up immediately after therapy. Of the remaining 125, 52 (41.6%) required from one to four additional doses to control their disease. Their follow-up will be the subject of another report. The other 73 patients who were controlled with a single dose of  $^{131}\text{I}$  have been followed for a period of one to twelve years for a total of 275 patient-years of observation (mean 3.76 years).

One year after therapy 13 of 73 (18%) were already hypothyroid and each successive year showed a variable percentage of permanent hypothyroidism. From then on, the cumulative incidence of hypothyroidism continued rising steadily as shown in Fig. 1.



TABLE I

Distribution of Patients Treated	
Total patients treated with <sup>131</sup> I	173
Lost to follow-up	48
Remaining under observation	125
Patients requiring additional doses	52
Patients controlled with a single dose	73

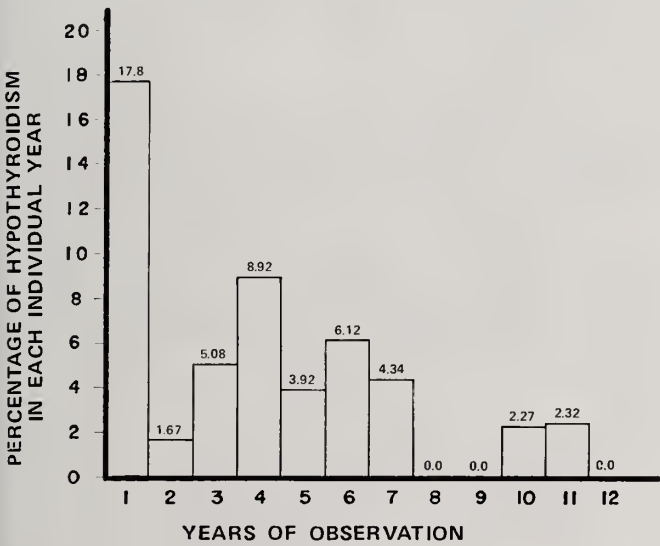


FIGURE 1

Percentage of Hypothyroidism per Year of Observation

Discussion

A review of the literature on the subject of hypothyroidism after <sup>131</sup>I therapy for hyperthyroidism yields only three series in which low doses were used with a follow-up period of at least 5 years.<sup>5-10</sup> The first one by Smith and Wilson, comes from England, the second one by Glennon, Gordon and Savin, from the United States and the third one by Cevallos, Hagen, Maloof and Chapman also from the United States. As may be seen in Table II, all show rather low percentages of hypothyroidism in the first year after treatment followed by a plateau up to 5 years in the first two series. Thereafter (Fig. II), the percentage in the second series rises steadily until it reaches 48% in 17 years. The third series shows an ascending curve parallel to ours but at a much lower level.

The percentage of hypothyroidism in our series is considerably higher than in the other three at each yearly interval despite the fact that the average dose of <sup>131</sup>I is comparable as can be seen in Table I. The yearly increment after the first year was 3.2% not much different from the other series.

TABLE II

Hypothyroidism and Approximate Dose <sup>131</sup> I			
Author	Approximate Dose mCi	Incidence of Hypothyroidism in 1 year or less %	Mean Annual Increment of Hypothyroidism after first year
Smith, 1967	3	12	0.0
Glennon, 1972	3	4	3.4*
Cevallos, 1974	3.6	8	3.8**
Present Series, 1981	3.47	18	3.2

\* After the 5th year  
\*\* Calculated from Figure 2

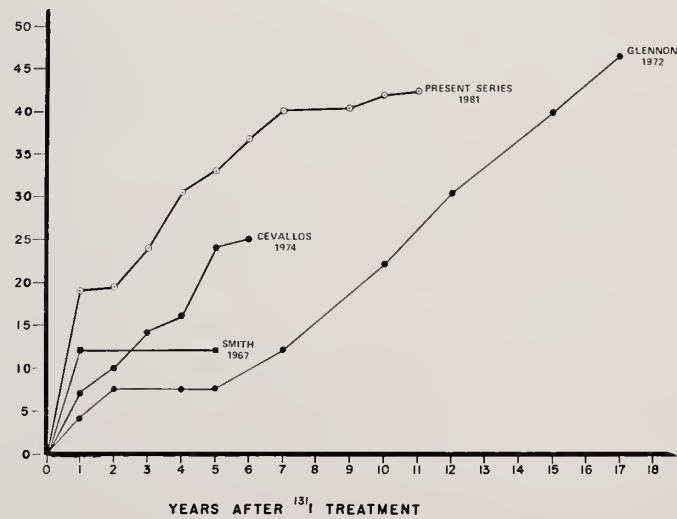


FIGURE 2

Cummulative Incidence of Hypothyroidism Following Low-Dose of <sup>131</sup>I

Conclusions

For many years we have suspected that for some unknown reason Puerto Ricans are more sensitive to the effects of radiation, at least with <sup>131</sup>I, than most people from the United States, Canada, Western Europe and South America. Our preliminary findings seem to support this hypothesis. We are waiting for the results of similar studies in other institutions and will continue this investigation for the next few years.

**Resumen:** Durante el período de 1968 a 1980, 173 pacientes con hipertiroidismo, todos menos 4 por enfermedad de Graves, fueron tratados con radioyodo  $^{131}\text{I}$  en el Hospital Municipal de San Juan. Cuarentiocho (28%) se perdieron a seguimiento y 52 (41.6 de los restantes 125) requirieron más de una dosis. Los restantes 73, tratados con una dosis promedio de 3.47 mCi (3-5 mCi), han sido supervisados desde uno a 12 años para un total de 275 pacientes-años. Trece de estos (18%) desarrollaron hipotiroidismo durante el primer año post-tratamiento y el porcentaje acumulativo de esta condición aumentó a razón de 3.2% por año hasta llegar a 38% en 12 años. Estas cifras son bastante más altas que las informadas por otros investigadores usando dosis bajas de radioyodo parecidas a las nuestras. Si estos hallazgos son confirmados por otros estudios similares, esto sugeriría que existe una mayor sensibilidad a los efectos de la radiación por  $^{131}\text{I}$  en la población puertorriqueña.

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# Pregnancy in the Hyperthyroid Patient

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**Summary:** Fifty hyperthyroid women were followed through 73 pregnancies on medical treatment only. In 25 instances they were euthyroid under medication while in the other 48, hyperthyroidism was present either with (12) or without (36) medication at conception. Five of 14 maternal complications were purely obstetrical and 8 of the remaining 9 occurred in patients who remained toxic throughout pregnancy. Total fetal loss was 14 of 76 (there were 3 twin pregnancies), 4 of them abortions due to obstetrical causes in 2 women euthyroid on medication. Of the remaining 10, 7 occurred among the 20 women who remained toxic. There were 2 neonatal deaths attributed to prematurity and one case of neonatal Graves' disease. There were no other goiters and no clinical evidence of hypothyroidism among the newborn. Maternal hypothyroidism was carefully avoided throughout all pregnancies.

Pregnancy is supposed to be a rather infrequent occurrence in the hyperthyroid woman. When it does occur it is usually in the patient rendered euthyroid under medication or, less often, it precipitates the onset of thyrotoxicosis. Rarely, "an occasional patient will become pregnant despite antecedent untreated hyperthyroidism".<sup>1</sup> Whatever the sequence of events, each patient presents a problem of individual management.

The objectives of therapy are to control the patient's hyperthyroidism and prevent or treat possible complications without affecting adversely the development of the fetus. The means to achieve these objectives, however, are various and during the past decades there has been ample debate about the merits of medical management versus thyroidectomy. We have preferred medical management and consider surgery only as a last resort. Thus, the purpose of this communication is only to present our experience and not to establish comparisons between different types of management and their results.

## Materials and Methods

From 1952 through 1979 fifty hyperthyroid women have been followed through 73 pregnancies. Contrary to what has been published in the North American literature<sup>1-5</sup> most of the 73 pregnancies (48 or 65.8%) occurred while the patients were toxic, even though 12 subjects were under antithyroid therapy. In the other 25 instances, the women were euthyroid while on medication (Table I).

In twenty-two instances the patients remained toxic throughout most of their pregnancies probably because many of them were first seen by us in the third trimester, plus the fact that one of them did not take the medication regularly or did not respond to medication.

All patients were hyperthyroid by the usual diagnostic parameters and all but one had Grave's disease. The exception had a hyperfunctioning nodule. All were treated with methyl-mercapto-imidazole (MMI) in divided doses ranging from 30 to 120 mg. daily, except in the second pregnancy of one patient, where propyl thiouracil (PTU) was used since she had not responded satisfactorily to MMI during her first one; during the third trimester of a second patient when neither drug was effective; and during both pregnancies of a third patient who was allergic to MMI. One patient inadvertently received a therapeutic dose of I<sup>131</sup> twice during the first few weeks of her third and fourth pregnancies, apparently without untoward effects.

Care was taken to follow the patients closely and to prevent hypothyroidism due to overdosage.

TABLE I

	At Conception	At Termination of Pregnancy
Euthyroid on Medication	25	53
Toxic on Medication	12	20
Toxic Without Medication	36	0
Total	73	73

## Results

Maternal complications are shown in Table II. All four cases of thyrotoxic heart disease with congestive failure plus the lone thyroid storm occurred among the 20 women who remained toxic throughout their pregnancies. Toxemia and eclampsia also occurred in 2 out of 20 toxic patients (10%) as against 1 in 53 (1.9%) among those who were euthyroid. The remaining complications were purely obstetrical and too few to be significant.



TABLE II

Maternal Complications			
	Euthyroid (53)	Toxic (20)	Total (73)
1. Thyrotoxic Heart Disease with Congestive Failure	0	4	4
2. Rheumatic Heart Disease	0	1	1
3. Thyroid Storm	0	1	1
4. Toxemia and Eclampsia	1	2	3
5. Premature Rupture of Membranes	1	1	2
6. Abruptio Placenta	0	1	1
7. Placenta Previa	0	1	1

The outcome is tabulated separately for the 70 single and 3 twin pregnancies (Table III). Total fetal loss was 13 in the first group with 11 abortions, but four of these appear to be unrelated to the thyroid condition. One was due to placenta previa and the other three occurred in the same patient, the first two attributed by obstetricians to incompetent os and the last one following a right nephrectomy. Both patients were euthyroid at the time of the abortions. Six of the other seven abortions occurred in very toxic women, one of them during a thyroid storm. When the 4 previously mentioned cases are excluded, we obtain an over-all corrected fetal loss of 9 out of 70 pregnancies or 13%.

If this total loss is analyzed separately it turns out to be 7 in 20 (35.0%) women remaining toxic and 3 in 49 (6.1%) whose thyrotoxicosis was controlled throughout their pregnancies.

TABLE III

Outcome of Pregnancy			
A. Single Pregnancies (70)	Euthyroid (50)	Toxic (20)	Total (70)
Full-term Live	40	8	48
Premature Live	4	5	9
Full-term Stillborn	1	0	1
Premature Stillborn	0	1	1
Abortions	5	6	11
B. Twin Pregnancies (3)	Euthyroid	Toxic	Total
	(3)	(0)	(3)
Full-term Live	2-1/2	0	2-1/2
Full-term Stillborn	1/2	0	1/2

Regarding the conditions of the offspring, 2 of 9 premature babies died within 48 hours probably due to prematurity and one full-term girl developed neo-natal Graves' disease 2-3 days after birth. Her symptoms lasted for about 2-3 weeks and gradually disappeared along with a decrease of LATS in serum. There were no other goiters and no gross abnormalities in physical or mental development.

Discussion

As stated before, the objectives of the management of the pregnant hyperthyroid patient are clear and unanimously accepted. The means to attain these objectives, however, are something else. A review of the literature, most of it in obstetrical journals, shows conflicting opinions. Tabert et al<sup>5</sup> compare the series published up to 1970 and add their own, after which they reach the conclusion that surgery gives better results, by adding up very dissimilar groups of patients reported by different investigators, and calculating percentages from their results. In 1974, Emslander and coworkers<sup>6</sup> again reviewed the literature and added three more series, including their own, but wisely abstained from drawing any conclusions as to the choice of therapy.

In our opinion, the fallacy of any such comparison lies precisely in the fact that in most of the published series the groups are not comparable. Only patients whose thyrotoxicosis has been controlled will be submitted to surgery and it is this group which also shows the better results. As shown in the analysis of our data, all the non-obstetrical complications and all fetal losses but two, occurred among the 18 women who remained toxic and who would have never been operated upon. It remains to be demonstrated in a large enough series of patients managed by the same group in the same institution, all meeting the criteria for surgery and then randomly assigned to either thyroidectomy or continuing medical management, whether one method is significantly better than the other.

It should be emphasized again, that no matter what method is used to control the thyrotoxicosis, **maternal hypothyroidism** must be avoided. This is more feasible with medical management which permits a flexible dose adjustment of the antithyroid drug.

Conclusions

We believe that hyperthyroidism can be safely managed throughout most pregnancies with anti-thyroid drugs and that surgery should be avoided whenever possible in a pregnant woman.

Our experience suggests that both maternal complications and fetal loss are directly related to duration and severity of the hyperthyroid state.

**Resumen:** Cincuenta mujeres hipertiroideas fueron supervisadas a través de 73 embarazos bajo tratamiento médico solamente. En 25 casos las pacientes estaban eutiroides bajo tratamiento al momento de la concepción mientras que otras 48 estaban hipertiroideas con (12) o sin (36) medicamento. Cinco de 14 complicaciones maternas fueron

puramente obstétricas y 8 de las otras 9 ocurrieron en pacientes que permanecieron tóxicas a través de su embarazo. La pérdida fetal fue de 14 en 76 (hubo 3 embarazos gemelares), 4 de ellos debido a aborto espontáneo por causas obstétricas en dos pacientes eutiroides bajo tratamiento. De las 10 restantes, 7 ocurrieron entre las 20 pacientes que permanecieron tóxicas. Hubo 2 muertes neonatales atribuidas a prematuridad y un caso de enfermedad de Graves neonatal. No hubo bocio ni evidencia de hipotiroidismo en los restantes neonatos. El hipotiroidismo materno fue cuidadosamente evitado.

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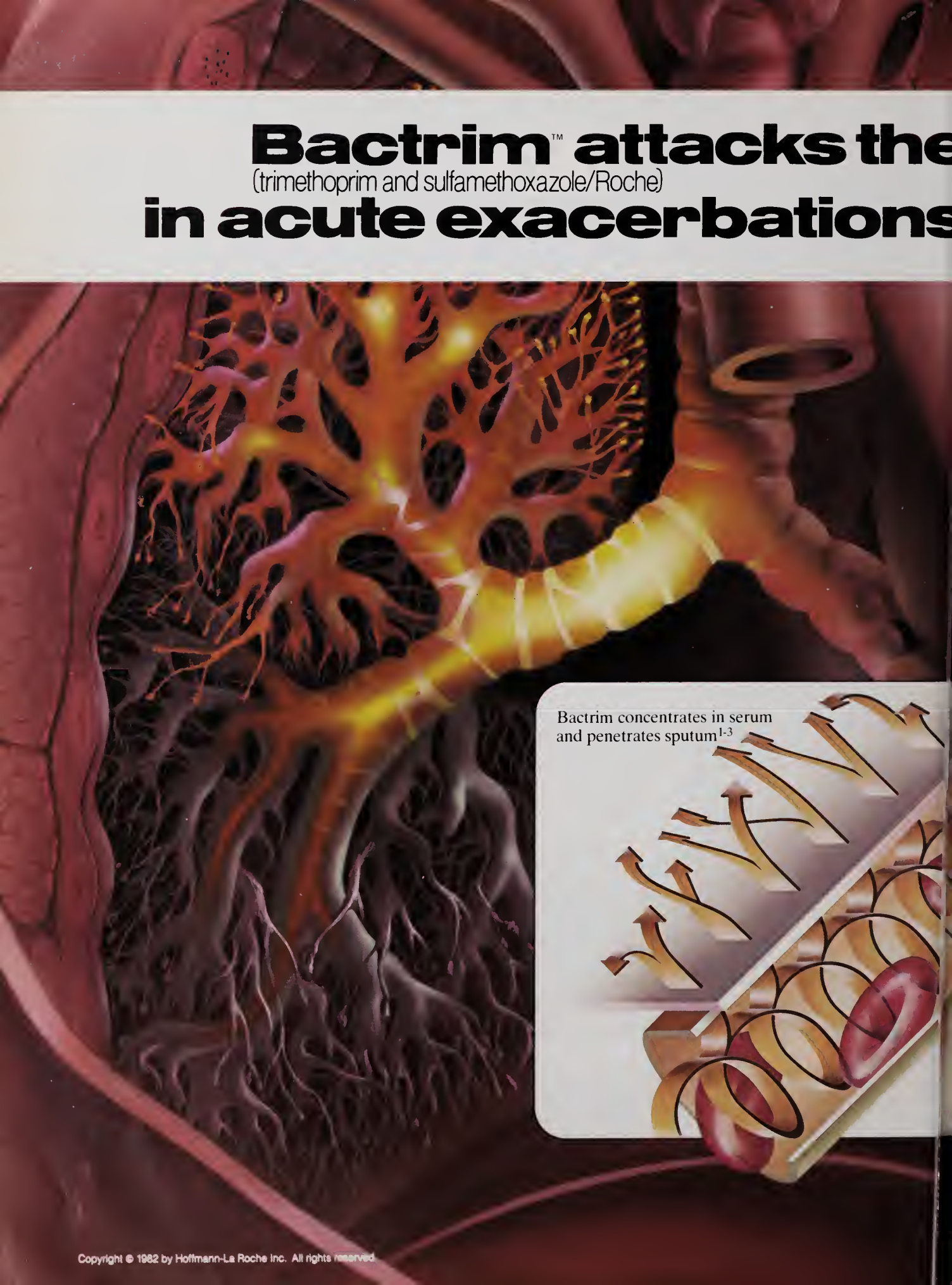
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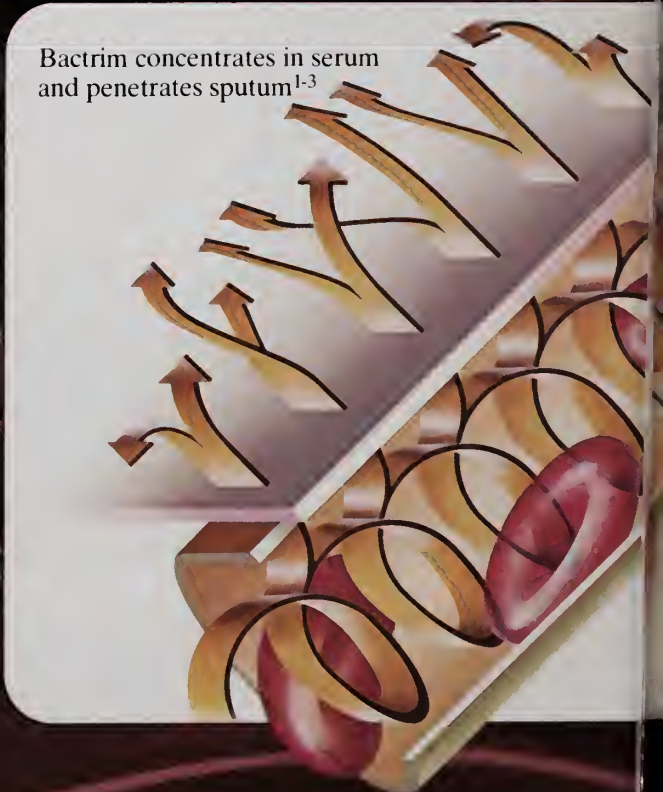
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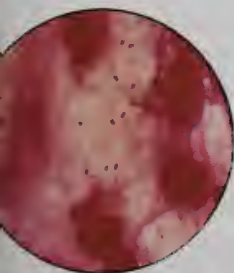
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For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.

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Also for the treatment of documented *Pneumocystis carinii* pneumonia.

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**Children:** Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

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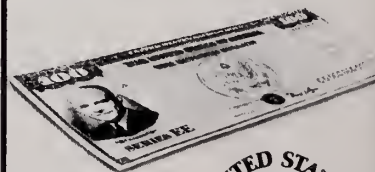
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# Thyroid Gland Suppressibility in Patients Treated with Radioiodine for Diffuse Toxic Goiter

Francisco L. Burgos, M.D.  
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**Abstract:** Twelve euthyroid patients previously treated with  $^{131}\text{I}$  for Graves disease were evaluated. The thyroid suppression test was judged to be able to indicate complete remission of the disease, but this did not correlate with clinical status, since six subjects who did not suppress were clinically euthyroid. On the other hand, serum TSH levels were valuable to determine subclinical hypothyroidism.

The thyroid gland uptake of radioiodine can be suppressed with exogenous sodium liothyronine administration in the normal person. Contrary to this, diffuse toxic goiter is characterized by non-suppressibility of the thyroidal uptake of radioactive iodine.<sup>1</sup> Antithyroid drug therapy may be associated with the return of suppressibility of the thyroid gland which correlated with a high incidence of long term remission following cessation of treatment.<sup>2</sup>

The significance of the thyroidal suppression test in patients on remission from Graves' disease after therapy with radioiodine has not been systematically determined. Alford reported a 72% non-suppressibility in 47 patients<sup>3</sup> out he included several patients that were clinically hyperthyroid. Suematsu evaluated 49 clinically euthyroid patients who had been treated for hyperthyroidism, but only 15 of them received radioiodine. The others received antithyroid medication or surgery. Eighteen of the 49 patients were suppressed with sodium liothyronine ( $\text{T}_3$ ), but he does not specify their mode of therapy.<sup>4</sup>

The present study was designed to evaluate the thyroid suppression test among clinically euthyroid patients after  $^{131}\text{I}$  therapy for diffuse toxic goiter and to determine if the serum thyrotropin levels correlated with suppressibility.

## Materials and Methods

Twelve clinically euthyroid patients previously treated with  $^{131}\text{I}$  for diffuse toxic goiter were studied. All were male patients with their ages ranging from 25 to 50 years (Table I). All of them received their therapy 18 months or longer prior to

this evaluation. The duration of clinical remission ranged from one to ten years. Thyroid status was evaluated clinically and by the determination of serum thyroxine ( $\text{T}_4$ ), Triiodothyronine ( $\text{T}_3$ ), Thyrotropin (TSH), and the 24 hr. thyroid uptake. The 24 hour thyroidal uptake was measured using 5 microcuries  $^{131}\text{I}$  orally. Sodium liothyronine ( $\text{T}_3$ ) 25 micrograms three times a day was then administered for seven days and the serum  $\text{T}_4$ , TSH and 24 hour  $^{131}\text{I}$  uptake were repeated.<sup>1</sup> Suppression was defined as positive if the final uptake was less than 50% of the uptake prior to  $\text{T}_3$ .<sup>1-5</sup> Informed consent was obtained from all subjects after the nature of the procedures had been fully explained. Serum  $\text{T}_4$ ,  $\text{T}_3$  and TSH were determined in the basal state in ten normal controls for comparison.

The serum  $\text{T}_4$  determinations by radioimmunoassay using Nuclear Medical Laboratory  $\text{T}_4$  Tetra Tab Kit were performed according to the method described by Chopra.<sup>6</sup> The serum  $\text{T}_3$  by radioimmunoassay using Abbott Laboratory Kit according to the method described by Hara.<sup>7</sup> The serum TSH by radioimmunoassay using Abbott Laboratory Kit was performed according to the method described by Odell.<sup>8</sup> Student "t" test analysis was utilized where appropriate.

TABLE I

Age Distribution of the Patients		
Age in Years	Number	Percent
20-30	2	16.6
31-40	1	8.4
41-50	6	50.0
51-60	3	25.0

## Results

The characteristics of the subjects studied are shown in Table 2.

Six of twelve patients (50%) showed non suppressibility of  $^{131}\text{I}$  uptake by  $\text{T}_3$ . Suppressibility bore no significant correlation to baseline serum  $\text{T}_3$ ,  $\text{T}_4$  or TSH (Table 3).

The TSH concentration was less than 4.8 micro IU/ml in five of the twelve patients prior to suppression with  $\text{T}_3$ . After one week of therapy with  $\text{T}_3$ , TSH decreased to below 2.8 micro IU/ml in all but two patients. One of the two patients had his uptake of  $^{131}\text{I}$  suppressed with liothyronine. Suppression occurred in three of seven patients with elevated TSH level and in three of five with low TSH level. There was no statistical significance between the level of TSH and serum  $\text{T}_3$ ,  $\text{T}_4$  and suppressibility (table 4).

No significant difference was found as to patient's age, interval between therapy, total  $^{131}\text{I}$  dose, number of doses and suppressibility.

TABLE II

DATA ON PATIENTS STUDIED								Post Liothyronine Suppression		
Pt.	Age	No Dose	<sup>131</sup> I Total mC Dose	T <sup>3</sup> microg/dl	T <sup>4</sup> microg/ml	TSH micro IU/ml	Uptake %	T <sup>4</sup> microg/dl	TSU micro IU/ml	Uptake %
1	48	1	5	163	9.8	20.4	19	7.8	0.4	12
2	47	1	3.6	127	9.5	3.9	19	6.2	0.4	6
3	54	1	3.0	48	8.2	20.5	16	8.5	2	8
4	46	1	3.5	145	6.5	6.7	32	6.2	0.3	23
5	60	1	3.0	127	8.6	23.0	18	8.5	1	8
6	59	1	3.0	118	6.8	1.2	11	6.2	0.9	0
7	29	1	3.1	116	8.9	8.6	30	7.4	2.8	13.2
8	28	2	8.4	115	5.8	39.5	21	6	18	9
9	46	1	2.5	88	5.6	39.5	22	5.9	7	15
10	44	1	2.3	118	7.6	0.3	20	9.1	0.3	16
11	44	3	12.5	192	9.6	2.5	18	10.3	0.4	10
12	39	1	3.7	118	7.9	4.8	15	8.8	1	8.6

12 pts.  $45 \pm 8.1$      $122.91 \pm 34.35$      $7.81 \pm 36$      $14.25 \pm 11.3$      $20.08 \pm 3.72$

$10.7 \pm 2.9$

10 controls 25-50     $144.5 \pm 45.3$      $9.38 \pm 1.50$      $1.33 \pm 0.91$

TABLE III

Suppressibility of the Thyroid Gland in Relation to Serum T <sub>4</sub> , T <sub>3</sub> and TSH Levels			
	T <sub>3</sub> ng/dl	T <sub>4</sub> microg/dl	TSH micro IU/ml
Controls n=10	$144.5 \pm 45.3$	$8.38 \pm 1.50$	$1.33 \pm 0.91$
Suppressed n=6	$129.4 \pm 16.03$	$7.92 \pm 1.39$	$15.24 \pm 14.37$
Not Suppressed n=6	$158.0 \pm 34.6$	$7.83 \pm 1.51$	$12.43 \pm 13.87$



TABLE IV

Serum TSH Level in Relation to T <sub>3</sub> , T <sub>4</sub> and Suppressibility of the Thyroid Gland				
	TSH micro IU/ml (x ± SEM)	T <sub>3</sub> ng/dl (x ± SEM)	T <sub>4</sub> microg/dl (x ± SEM)	No. of Patients that suppressed
Control n=10	1.33 ± 0.91	144.5 ± 45.3	8.38 ± 1.50	—
Low TSH n=5	2.54 ± 1.65	159.5 ± 30.57	8.28 ± 1.09	3
High TSH n=7	23.10 ± 13.15	133.0 ± 26.32	7.53 ± 1.63	3

### Discussion

In this study we found that 50% of the patients did not suppress the thyroidal uptake of <sup>131</sup>I after the exogenous administration of T<sub>3</sub>. None of our patients were hyperthyroid. All of our patients were on clinical remission of their disease, although seven of twelve had sub-clinical hypothyroidism as manifested by the elevated serum TSH. It is interesting to note that elevated serum thyrotropin levels were found in patients with normal serum T<sub>3</sub> and T<sub>4</sub>. This finding concurred with those published by others.<sup>3 9 10</sup> Also there was no correlation between thyroid suppressibility and serum thyrotropin levels. Therefore, the thyroid stimulating hormone was not a major determinant of thyroid suppression. Previous studies which searched for the presence of elevated long acting thyroid stimulators (LATS) titers in patients with thyroid non-suppressibility<sup>3 5</sup> failed to demonstrate correlation between suppression and circulating LATS. Non suppression could not be explained either by the hyperplastic appearance of the thyroid acinar tissue remaining several years after irradiation as reported by some investigators<sup>11 12</sup>, as other investigators have reported a diminution of follicular size in nearly all glands after irradiation.<sup>13</sup>

Since serum TSH, LATS or the pathological changes involved cannot explain the suppressibility of the thyroid gland after radioiodine therapy, we postulate that the patients who suppressed were in complete remission of their disease, as in the case in those who suppress after antithyroid drug treatment. Those who failed to suppress were probably not in full remission, but they were euthyroid because the radioiodine effectively reduced the serum thyroxine levels either by cell destruction or by reducing the synthesis of the hormone.<sup>14</sup>

Our present study and previous findings on TSH levels after <sup>131</sup>I therapy<sup>4 9 10</sup> provide evidence that this test is most valuable for predicting which patients will subsequently develop hypothyroidism. On the other hand, the only information that can be obtained with the thyroid suppression test in patients treated with <sup>131</sup>I for Graves is the determination of complete remission. This information has no clinical significance since it does not necessarily correlate with the clinical picture.

**Resumen:** Doce pacientes eutiroides tratados anteriormente con <sup>131</sup>I para la enfermedad de Graves fueron evaluados. La prueba de supresión tiroidea corroboró en seis de estos una remisión completa de la enfermedad. No obstante, dicha prueba no correlaciona con la condición clínica ya que el 50% de ellos no suprimieron y estaban clínicamente eutiroides. Por otro lado, el nivel sérico de TSH fue sensitivo en determinar hipotiroidismo subclínico.

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# Hermafroditismo Verdadero: Presentación de Tres Casos y Revisión de la Literatura

Carlos J. Cintrón Ortiz, MD\*

El Hermafroditismo Verdadero se caracteriza por la coexistencia de tejido gonadal de ambos sexos, o sea, ovario y testículo. La apariencia fenotípica puede ser de cualquiera de los dos sexos (aunque a veces anómala e incompleta) y los genitales externos e internos pueden variar desde los de una hembra normal a los de un varón normal, (ver figura número 1). El tejido gonadal puede ser testículo y ovario por separado o combinados en ovotestes.



Figura 1

Relativamente pocos casos han sido estudiados por completo y es solo recientemente que se han podido suplementar los hallazgos clínicos y patológicos con estudios citogenéticos. De los casos reportados, un poco más de 200, se ha establecido el cariotipo del paciente en solo algunos 60-70 de éstos. Muchos de estos pacientes se han criado como varones y el diagnóstico rara vez se ha hecho antes de la pubertad. Algunos de estos "varones" se han presentado con hemorragia vaginal, "hematuria" o ginecomastia (supuestamente por estrógenos

producidos en el ovario). Usualmente las gónadas se encuentran en la cavidad abdominal pero a veces el testículo u ovotestes aparece herniado en la región inguinal.

Además de revisar los casos previamente reportados en la literatura, presentamos cuatro casos nuestros debidamente evaluados y en los cuales confirmamos el diagnóstico de Hermafroditismo Verdadero. Estos pacientes fueron referidos al Centro Médico de Puerto Rico por presentar algunas o todas las manifestaciones antes expuestas. En 3 de ellos se comprobó por patología la existencia de ambos: tejidos ovárico y testicular, confirmando de esta forma el diagnóstico de Hermafroditismo Verdadero. El cuarto paciente fue evaluado inicialmente en marzo de 1981 a la edad de 3 meses y aún no se le ha hecho laparatomía exploratoria. Todas las pruebas hormonales y otros estudios específicos para descartar problemas adrenales y otras etiologías diversas causantes de genitales ambiguos fueron realizados y reportados normales antes de proceder a la laparatomía exploratoria. La Tabla I resume los datos relevantes de cada paciente.

TABLA I

Pacientes Hermafroditas Verdaderos Estudiados en el Centro Médico de Puerto Rico				
PACIENTE ADM	M H H Julio 1967	M F M Octubre 1969	J O F Octubre 1972	J C O Marzo 1981
EDAD	3 meses	20 años	4 1/2 meses	3 meses
CRiado COMO	Hembra	Varón	Varón	Varón
RAZON DE REFERIDO	Genitales ambiguos	Ginecomastia bilateral Pene hipospádico pequeño Hematuria Cirugía correctiva para hipospadia de 3er grado a los 7 años de edad	Falo hipospádico de 3er grado Criptorquidismo izq. Masa inguinal der	Genitales ambiguos
HALLAZGOS AL EXAMEN FISICO	Falo hipospádico de 3 cm de longitud Seno urogenital Fusión labias mayores Masa palpable en labia derecha Examen uretroscópico reveló vagina, útero, trompas de Falopio	Ginecomastia bilateral Pene hipospádico pequeño Escroto bifido Seno urogenital Hernia inguinal	Falo hipospádico bilateral Fusión de pliegues labia escrotales Masa labia derecha Gónada izq. no palpable	Falo hipospádico Seno urogenital Saco escrotal derecho Masa en escroto derecho de 1.75 cm. Ausencia de gónada izq. palpable
CROMATINA SEXUAL	7%	Positiva	42%	Cromatina sexual - 10% Cuerpo y - 30%
CARIOTIPO	46, XX/46, XY/47 XXY	46, XX	46, XX	
HALLAZGOS OPERATORIOS	Útero, vagina normal T. de Falopio Bil Ovotestes izq. intra-abdominal En lado derecho ovario intra-abdominal y un ovotestes con estructuras ductales herniado en labia	Útero hipoplástico Ovotestes derecho herniado No se encontró gónada izquierda	Testículo en pliegue labio-escrotal derecho unido a cordón espermático que llegaba a un útero hipoplástico Ovario izquierdo intraabdominal	
OPERACION REALIZADA	Extracción ambos ovotestes Recesión del clitoris hipertrofiado Vaginoplastia	Extracción derecho Mastectomía bilateral	Extracción testículo derecho. Recesión clitoris hipertrofiado Vaginoplastia	
SEXO FINAL ADJUDICADO	Hembra	Varón	Hembra	Varón

NOTA: A estos pacientes no se les hizo estudios serológicos para la presencia del antígeno H Y

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Discusión

Merriell y Ramsey revisaron ciento catorce (114) casos de Hemafroditismo Verdadero en el 1963. En estos casos se distinguieron tres situaciones gonadales: (Ver figura número 2).

- 1. 22 casos laterales - testículo en un lado y ovario en otro.
- 2. 26 casos bilaterales - testículo y ovario u ovotestes en cada lado.
- 3. 41 unilaterales - ovotestes en un lado y testículo u ovario en el contralateral.

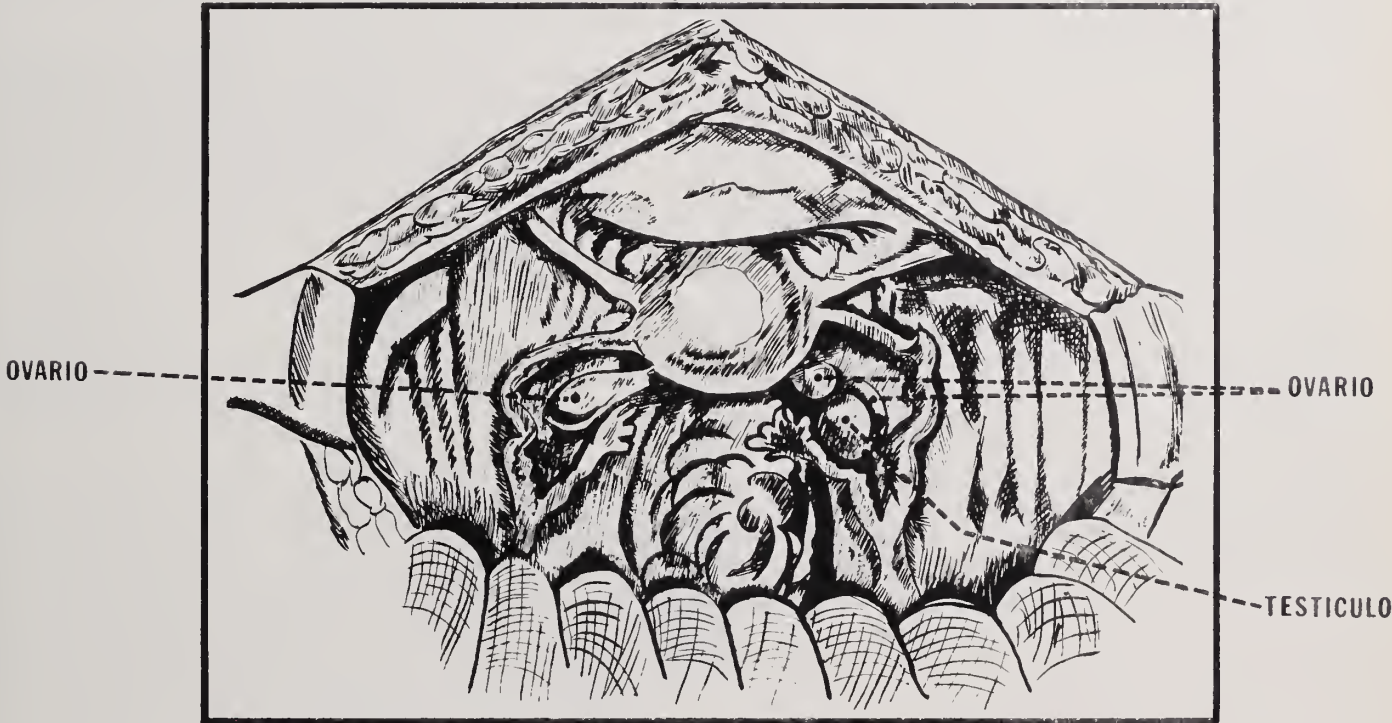


Figura 2



Estructuras externas e internas de un hermafrodita verdadero

En 25 casos los hallazgos eran desconocidos.

La laparatomía exploratoria ha revelado en la mayoría de los casos un útero (hipoplástico o normal), pero la diferenciación de los otros ductos genitales usualmente corresponde a la naturaleza de la gónada adyacente (Guinnet, 1965). Aunque la expresión fenotípica varía desde completamente masculina, el 75% de los pacientes son predominantemente varones en apariencia. En los sujetos que fenotípicamente son predominantemente varones es común la hipospadia con o sin criptorquidismo. Si hay una gónada herniada en la región inguinal ésta usualmente es un testículo o un ovotestes, 63%. La gónada con predominio ovárico rara vez se encuentra extra abdominal.

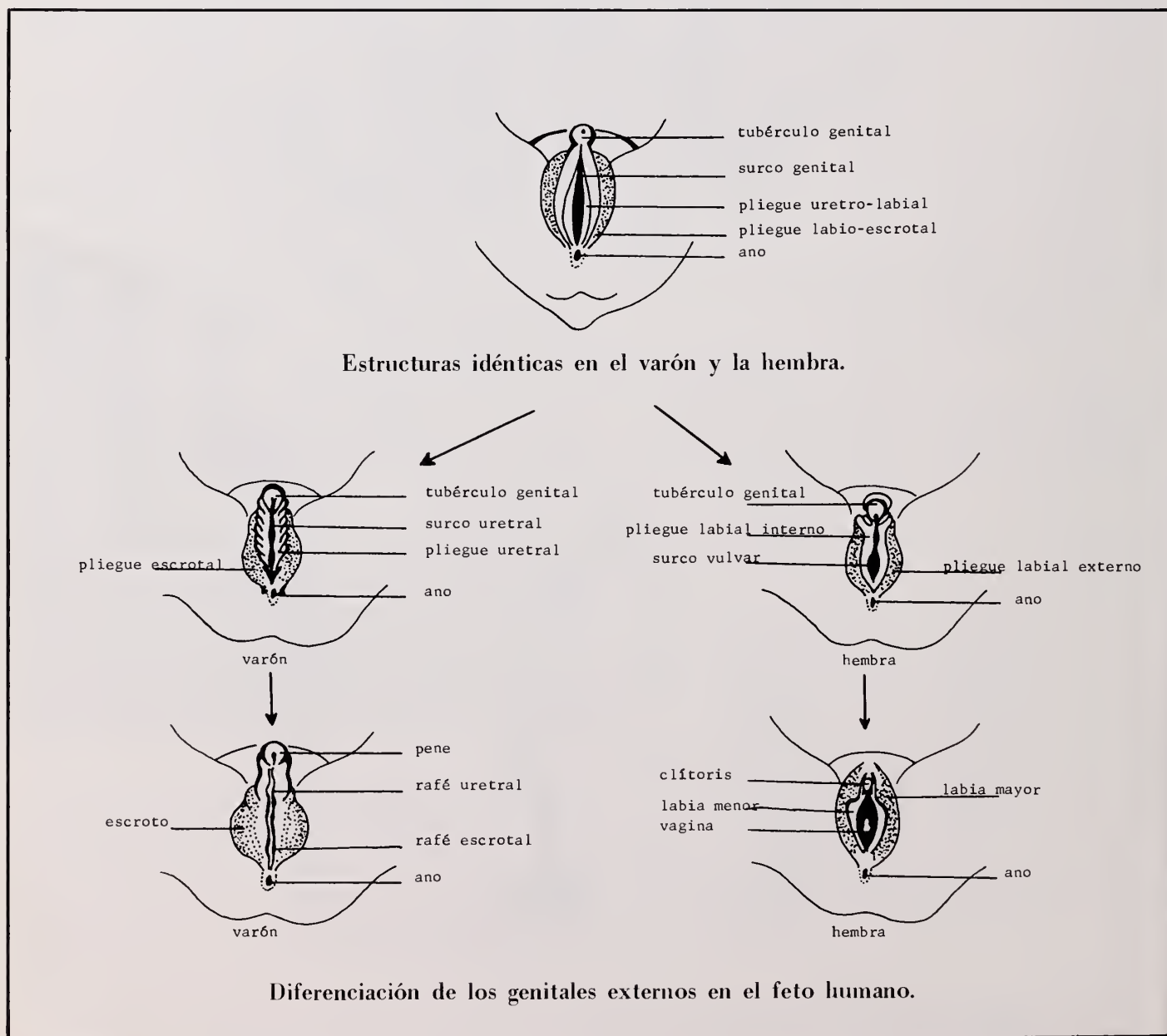
A tres cuartas partes de los casos reportados se le ha asignado el sexo de varón al nacer y así han sido criados. La presencia casi constante de útero en estos pacientes sugiere

que la hormona responsable de la diferenciación externa (andrógenos), predomine funcionalmente sobre las sustancias inhibitoras del ducto mulleriano, del cual se origina el útero, trompas de Falopio y tercio superior de vagina.

Hay ciertas claves importantes que nos pueden orientar en cuanto a un dominio testicular incompleto; (ver figura número 3).

1. Hipospadia, que resulta del fallo en fusión de los pliegues uretro-labiales que son los responsables de mover el meato uretral ventralmente hacia la punta del pene.
2. Deficiencia parcial o completa en la fusión de los pliegues labio-escrotales.
3. Criptorquidismo.
4. Hernia inguinal.

Figura 3





Ya en la adolescencia un 80% de estos "varones" desarrollan ginecomastia y 50% tienen menstruaciones cíclicas (interpretadas como hematuria). Funcionalmente el tejido ovárico de estos pacientes predomina sobre el testicular. Se ha demostrado ovulación en más de un 25% de los casos pero la espermatogénesis es rara. Los hallazgos de laparotomía en general reflejan la incompetencia del testículo embrionario en suprimir el desarrollo mülleriano y estimular el wolffiano.

Desde el punto de vista citogenético el 80% de los hermafroditas verdaderos tienen cromatina sexual y cuerpos de Barr positivos (para un sexo genético femenino). La literatura reporta un 53-65% con cromosomas sexuales 46,XX. Alrededor de un 5% tienen cromosomas sexuales XY. Los restantes son mosaicos; por ejemplo:

45,X0/46,XY  
46,XX/47,XXY  
46,XX/47,XXX  
46,XX/48,XXYY  
46,XX/46,XY/47,XXY  
46,XY/47,XXY/49,XXYYY

El hecho de que en la gran mayoría de los hermafroditas verdaderos solo se pueda demostrar una línea celular con cromosomas sexuales XX está en discordancia con evidencias establecidas que sugieren la presencia del cromosoma Y como necesaria para inducir la formación de un testículo de una gónada embrionaria indiferenciada. Esto se ha tratado de explicar de la siguiente forma:

1. La mayoría de los cariotipos se hacen de sangre periférica. Podría haber una línea celular XY confinada en el tejido testicular y aún más específicamente en las células germinales primitivas (que no crecen en el cultivo).
2. Ferguson - Smith (1966) sugirió que la pareja de X representaría una X normal y la otra contendría el material genético del cromosoma Y determinante de la formación del testículo. Se explicaría esto a base de un intercambio X-Y durante la meiosis, la porción de Y necesaria para la inducción del desarrollo testicular sería pequeña y podría haber translocación sin cambio cariotípico.
3. Doble fertilización de un óvulo por dos espermatozoides o la fusión de dos óvulos.
4. Desaparición de la línea XY que existió en vida embrionaria.

Estudios recientes sobre el antígeno H-Y (antígeno organizador testicular), revelan que el control genético en la diferenciación gonadal actúa a través de la expresión del gene H-Y que se asocia normalmente al cromosoma Y. Mutaciones que interfieran con estas correlaciones resultan en forma de intersexualidad como el Hermafroditismo Verdadero. (Ohno, Wachtel, Fraccaro).

## Conclusión

Es de suma importancia tener siempre en mente esta entidad al encontrarnos con pacientes que presentan alguna ambigüedad de los genitales externos como hipospadia, criptorquidismo uni o bilateral, escroto bífido, etc. Todos ellos ameritan estudios citogenéticos y hormonales para un diagnóstico correcto y manejo adecuado tempranamente.

**Resumen:** Alrededor de 200 casos de Hermafroditismo Verdadero han sido reportados en la literatura. En sólo algunos 60-70 de éstos se han suplementado los hallazgos clínicos y patológicos con estudios citogenéticos. Muchos de estos pacientes han sido criados como varones y el diagnóstico se ha hecho después de la pubertad. En la mayoría de ellos se ha encontrado un útero al hacerle laparotomía exploratoria. Si fenotípicamente son predominantemente varones es común la hipospadia y si hay una gónada herniada ésta es usualmente testículo u ovotestes. En la adolescencia un 80% desarrolla ginecomastia y un 50% tiene menstruaciones cíclicas. El 80% tiene cromatina sexual positiva y en el 60% sus cromosomas sexuales son XX. Hemos presentado cuatro pacientes con Hermafroditismo Verdadero estudiados en el Centro Médico de Puerto Rico cuyos hallazgos clínicos, patológicos y citogenéticos concuerdan con lo descrito previamente en la literatura médica.

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# Aspiración con Aguja Fina de los Nódulos Hipofuncionantes del Tiroides

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**Resumen:** Se presenta la experiencia con la biopsia por aspiración con aguja fina en 35 pacientes con nódulos hipofuncionantes de tiroides. En 24 de ellos se obtuvo material para estudio histológico postquirúrgico que permite hacer correlación con los estudios citológicos previos. Aunque en sólo 30 de las 35 biopsias por aspiración (86%) se obtuvo material adecuado para diagnóstico citológico, éstos incluyen los 24 casos operados. Se encontraron 7 lesiones malignas (29%) y 17 benignas.

De las 20 lesiones cuya biopsia por aspiración fue informada como negativa para malignidad, 4 (20%) fueron falsamente negativas.

Sólo en 3 de las 7 neoplasias malignas (43%) se detectó el cáncer por la citología, lo cual corresponde a una baja sensibilidad para la prueba en estudio. Sin embargo sólo uno de los 17 nódulos que fueron benignos en la operación dió un resultado falsamente positivo lo cual corresponde a una especificidad del 94%.

Ninguno de los pacientes tenía antecedentes de irradiación al cuello y no hubo complicaciones atribuibles a la biopsia.

## Introducción

En los últimos años se ha dado énfasis al diagnóstico por biopsia de las lesiones tumorales en múltiples sitios del cuerpo. Como la glándula tiroides es de fácil acceso para un procedimiento esencialmente atraumático como es la biopsia por aspiración con aguja fina, este procedimiento se ha popularizado especialmente en Europa. En lugares como Copenhague y en el Instituto Karolinska de Estocolmo se hacen biopsias a casi todo tipo de lesiones tiroideas. En Norte América ha habido cierto escepticismo hacia dicho método diagnóstico y sólo a fines de la década de los 70 comienzan a publicarse los resultados de varios investigadores quienes específicamente la han usado para estudiar lesiones nodulares de la glándula tiroidea.<sup>1,2,3,4,5</sup> La renuencia al uso de tal procedimiento aparentemente surgió, porque en los primeros estudios publicados en la literatura médica norteamericana utilizaban la aguja de Vim Silverman. Debido al calibre de dicha aguja, el procedimiento es menos atractivo, cuando se piensa que debe insertarse en un órgano situado en el cuello y cuando se tiene en cuenta que la lesión que se va a someter a biopsia tiene muchas veces solo unos

centímetros de diámetro. Por otro lado la morbilidad asociado con dicho instrumento es mucho mayor,<sup>1,5,6,7</sup> necesita considerable experiencia por parte del médico que la utiliza, y hay por lo menos un informe de implantación de tumor en el tracto producido por la aguja.<sup>8</sup>

En Puerto Rico no ha habido hasta el momento informes de uso de este método diagnóstico para ayudar al manejo clínico integral de los pacientes afectados por enfermedad nodular del tiroides. Con miras a acumular experiencia sobre la factibilidad y la utilidad del procedimiento en cuestión, se diseñó el presente estudio.

## Materiales y Métodos

A todos los pacientes adultos evaluados en la Sección de Endocrinología de este Hospital en el período comprendido entre Enero 1978 y Junio 1981 y que tenían diagnóstico de nódulo solitario hipofuncionante del tiroides, se les hizo biopsia por aspiración por medio de la técnica descrita más adelante. Todos ellos finalmente fueron enviados al Departamento de Cirugía para ser operados.

La evaluación inicial de cada paciente comprendió una historia clínica pertinente y un examen físico completo. A cada uno de ellos se le ordenó gammagrafía con <sup>131</sup>I y <sup>99</sup>Tc, captación en 24 horas de <sup>131</sup>I, ecografía del cuello y pruebas de función tiroidea (T<sub>3</sub>, T<sub>4</sub>, y TSH por radioinmunoensayo). Con lo anterior se pretendía excluir los pacientes con nódulos no solitarios (Bocios multinodulares) o los que tuvieran un nódulo único pero hiperfuncionante o normofuncionante. La aspiración de los nódulos se hizo en el paciente ambulatorio con la excepción de 6 casos que ya habían sido admitidos para escisión quirúrgica del nódulo por hemitiroidectomía. El paciente se colocaba en posición supina con el cuello hiperextendido y después de adecuada antisepsia del área y de anestesia intradérmica y subcutánea con xilocaína al 2% usando una jeringuilla de 1 cc y una aguja #25, se procedía a la aspiración-biopsia. Para ello se utilizaron agujas desechables #21 conectadas a una jeringuilla de 10 cc. Se hacía succión fuerte y momentánea (1-2 segs) del área afectada si el nódulo era sólido y el procedimiento se repetía 1-3 veces si era necesario. Si se trataba de un quiste o si se obtenía líquido del nódulo se procedía a drenarlo completamente si era posible. El material obtenido se extendía en laminillas de vidrio con una de sus caras rugosa, inmediatamente las laminillas se colocaban en un receptáculo provisto de alcohol etílico al 95% para una adecuada fijación. Como la mayoría de las veces el material obtenido de los nódulos sólidos no es aparente en la jeringuilla sino que queda dentro de la aguja, se usaba solución salina para expulsar el espécimen sobre la laminilla. Se hacía presión por varios minutos sobre el área biopsiada y se procedía a llevar las laminillas al Departamento de Citología para su procesamiento final por el método de Papanicolaou y ulterior lectura. Del material obtenido de los quistes, además de hacer extendidos en laminillas, se enviaba una parte o todo el fluido obtenido para, previa centrifugación, hacer un bloque celular y estudiarlo por medio de tinciones histológicas estandar. Unos días más tarde se refería el paciente al cirujano para ser sometido a la operación indicada en cada caso particular (hemitiroidectomía con istmectomía del lado afectado o tiroidectomía total). Tanto para la biopsia como para la

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*Este trabajo fue presentado el 18 de octubre de 1981, en la Asamblea Científica Anual de la Sociedad Puertorriqueña de Endocrinología y Diabetología celebrada en Dorado, Puerto Rico.*



operación quirúrgica se solicitó consentimiento escrito de los pacientes.

El cálculo de la sensibilidad y la especificidad de la prueba en estudio (biopsia por aspiración) se hizo convencionalmente partiendo de la definición de tales términos.<sup>9</sup> La sensibilidad mide la fracción de pacientes con la enfermedad que serán detectados por la prueba que se está estudiando.<sup>9</sup> Puede expresarse como el resultado de dividir el número de pacientes con enfermedad maligna cuya prueba es positiva por el total de pacientes con enfermedad maligna. Por otro lado, la especificidad mide la fracción de pacientes que verdaderamente no tienen la enfermedad.<sup>9</sup> Se expresa como el resultado de dividir aquellos pacientes con enfermedad benigna cuya prueba es negativa, por el total de los pacientes con enfermedad benigna. Es importante recalcar que el resultado de la biopsia no incidía en la decisión de operar o no, si no que todos los pacientes con nódulos fríos serían operados en ausencia de contraindicación médica o de algún otro factor que impidiera la operación (negativa del paciente por ejemplo).

### Resultados

De los 35 pacientes a quienes se hizo biopsia por aspiración con aguja, en 30 casos (o sea 86%) la muestra tomada fue catalogada por los citólogos como satisfactoria. Sin embargo, en todos los 24 pacientes que fueron operados el material obtenido previamente para estudio citológico fue calificado como adecuado y pudo ser finalmente comparado con el resultado histológico. En la Tabla I se tabulan los diagnósticos obtenidos en los 24 casos operados con énfasis en si la condición era o no benigna. Infortunadamente no pudo correlacionarse esto con las características sonográficas preoperatorias de la lesión, porque por múltiples razones solo se obtuvieron ecografías en 11 de esos pacientes. Diecisiete pacientes (70.8% del sub-grupo operado) tenían lesiones benignas, lo que deja 7 casos (29.2%) con lesiones malignas del tiroides. No hubo casos de carcinoma medular ni indiferenciado pero vale la pena citar que uno de los casos que tenía un carcinoma papilar se presentó 8 meses después de habersele hecho una hemitiroidectomía, con una metástasis que demostraba una histología de tipo indiferenciado de células gigantes completamente diferente de la inicial y murió 3 meses más tarde sin haber respondido a radioterapia externa ni quimioterapia.

En ninguno de los 24 pacientes operados había previa historia de irradiación al cuello.

De los 7 pacientes con cáncer, 6 han podido ser seguidos por un período de tiempo que oscila entre 12 y 23 meses y no hay en ellos evidencia de siembra del tumor en el área de la punción. Por otro lado vale anotar que con la excepción de un individuo con adenocarcinoma papilofolicular que tenía metástasis al cuello al presentarse originalmente y que recibió una tiroidectomía total exitosa, todos los otros 23 pacientes recibieron una hemitiroidectomía del lado afectado con istmectomía como es la conducta adoptada por nuestro Departamento de Cirugía para el manejo de los nódulos fríos del tiroides. De ellos solo 1 caso (la paciente de la transformación anaplástica) ha recaído hasta el momento y todos los demás son mantenidos en dosis supresivas de levotiroxina.

TABLA I

Histopatología de 24 Nódulos Hipofuncionantes del Tiroides		
Histología	Casos	Porcentaje
<b>Benignos</b>		
Bocio nodular	6	
Adenoma folicular	9	
Quiste coloide	1	
Tiroiditis linfocítica	1	
Total	17	70.8
<b>Malignos</b>		
Adenocarcinoma papilar	2	
Adenoma folicular mas focos de carcinoma papilar	3	
Carcinoma papilo-folicular	1	
Adenocarcinoma folicular	1	
Total	7	29.2
Gran total	24	100.0

En la Tabla II se muestran en forma comparativa los resultados de la biopsia por aspiración y el resultado patológico postoperatorio con respecto a si el diagnóstico obtenido era benigno o maligno. Se obtuvieron 4 resultados falsamente negativos (20%) y hubo un caso falsamente positivo. Visto de otro modo 16 de los 20 casos negativos citológicamente eran verdaderamente negativos (80%).

Finalmente de los 11 pacientes que no fueron operados 8 se perdieron el seguimiento y no sabemos por qué razón no se les operó. En los otros tres se omitió la operación por las siguientes razones: 2 de ellos tenían enfermedades concomitantes que contraindicaban relativamente la cirugía. Uno de ellos tenía biopsia negativa y en el otro el material era inadecuado para diagnóstico. El tercer paciente fue reevaluado y se consideró que el área "fría" que se había calificado inicialmente como un nódulo era un área de captación disminuida en una glándula con enfermedad de Hashimoto. Su biopsia era negativa para malignidad.

TABLA II

Comparación entre los Resultados de la Biopsia con Aguja Fina y la Histopatología Postquirúrgica en 24 Pacientes con Nódulos Hipofuncionantes*				
		Histología postquirúrgica		
		Negativa	Positiva	Total
Biopsia con Aguja fina	Negativa	16(a)	4	20
	Positiva	1	3(b)	4
	Total	17(x)	7(y)	24

\* (a): Negativo verdadero

(b): Positivo verdadero

(x): Total negativos

(y): Total positivos

## Discusión

En este trabajo hemos tratado de observar la utilidad de la biopsia por aspiración en el estudio de las lesiones nodulares tiroideas. Para ello los citopatólogos no conocían los hallazgos clínicos de cada paciente y por otra parte se planeó que el resultado de la biopsia no influenciaría en la decisión de operar al paciente con un nódulo frío.

Aunque nuestra serie no es grande, la presencia de 7 neoplasias malignas en un total de 24 nódulos fríos operados corresponde a una frecuencia de 29% (Tabla I) que es similar a la de 24% encontrado en Puerto Rico por Paniagua y colaboradores.<sup>10</sup> En la literatura médica norteamericana esta frecuencia es de 25% en promedio, con una oscilación entre 8 y 35%.<sup>11 12 13 14</sup>

Con los datos obtenidos pudimos estimar una sensibilidad de 43% y una especificidad de 94% (Tabla III). En el diagnóstico de lesiones malignas es importante que la prueba diagnóstica utilizada sea altamente sensible y altamente específica. Nuestros resultados nos dicen que la biopsia por aspiración con aguja fina de nódulos tiroideos cumple esta condición solo en cuanto a especificidad se refiere. Esto nos permite presumir que en acuerdo con tales resultados la cantidad de pacientes con lesiones benignas que enviaríamos para tiroidectomía sería pequeña. Sin embargo, como la prueba no es sensible esto podría inducir al clínico a omitir o posponer la eliminación de una lesión tumoral.

TABLA III

Especificidad y Sensibilidad para Cáncer de Tiroides de la Biopsia con Aguja Fina.**	
Especificidad	94%
Sensibilidad	43%

\*\* Especificidad  $\frac{a}{x}$  (ver Tabla II)

Sensibilidad  $\frac{b}{y}$  (ver Tabla II)

Debido al riego sanguíneo abundante que tiene la glándula tiroidea es posible aspirar sangre en un porcentaje alto de los casos y diluir por tanto la muestra obtenida. Por eso se ha enfatizado que la aspiración no dure más de 1-2 segundos.<sup>15</sup> Esta dilución es inevitable en las lesiones quísticas. Como ambas situaciones fueron frecuentes en nuestros casos, esto podría explicar en parte la baja sensibilidad obtenida en nuestro estudio que está en desacuerdo con los resultados publicados en la literatura donde se ha encontrado una correlación entre los hallazgos operatorios y la citología previa por aspiración que oscila entre 65% y 95%.

Finalmente podemos decir que este estudio preliminar realizado en un hospital general nos indica que este procedimiento es factible en nuestro medio y no conlleva morbilidad con la técnica empleada. Sin embargo, en el estado actual de nuestra experiencia un resultado negativo (y esto es similar a lo publicado en la literatura) no permite descartar la tiroidectomía, lo cual sería altamente deseable en pacientes ancianos o

con complicaciones médicas que impliquen un riesgo quirúrgico alto. La decisión quirúrgica debe por tanto descansar en una ponderación de los datos clínicos y sonográficos, con la biopsia siendo de ayuda solo cuando es positiva.

## Reconocimientos

Los autores agradecen la colaboración del Dr. Luis Castillo que participó en la planeación del protocolo y tomó las primeras biopsias. La ayuda de la Sección de Citopatología del Centro Médico de Puerto Rico en especial de la citóloga Sra. Ruth Rodríguez y del técnico Sergio Alicea, fueron invaluable. Finalmente debemos reconocer el estupendo trabajo secretarial de las señoras Sara H. Ortiz y Gloria E. Lázaga.

**Abstract:** Thirty five patients with proven solitary hypofunctioning thyroid nodules underwent fine-needle aspiration biopsy. Satisfactory material was obtained in 30 cases (86%) including 24 who were subsequently operated upon, regardless of biopsy results. Malignant tumors were found in 7 (29%).

Of 20 lesions whose biopsy was reported as negative for malignancy, 4 (20%) were false negative. Of 7 lesions diagnosed as malignant by surgery only 3 were detected by biopsy indicating a sensitivity of 80%. On the other hand only 1 of 17 patients with benign lesions by surgery was interpreted as malignant by biopsy showing a specificity of 94%.

None of the patients had a history of previous neck irradiation and there were no complications following biopsy.

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# Resúmenes de La Literatura Médica

**EFFECT OF CIMETIDINE ON INTESTINAL ADAPTATION FOLLOWING MASSIVE RESECTION OF THE SMALL INTESTINE.** Tomas De La Vega, J.E., Barner, B.F., Haklin, M.S. et al *Surgery, Gynecology & Obstetrics* 157: 41, 1983.

The authors present their results of the treatment of massive resection (80%) of the small intestine with cimetidine, using a well constructed experimental canine model. They demonstrated several salutary effects of chronic cimetidine ingestion following massive resection of small intestine including control of gastric acid hyper-secretion. In addition they documented a reduction in steatorrhea and measured an accelerated intestinal adaptation using morphometric parameters which included length and width of villi and depth of the crypts of Lieberkuhn.

These results support to the use of cimetidine in the clinical treatment of the short bowel syndrome.

Pedro J. Rosselló, M.D. F.A.C.S.

**LOS EFECTOS DE LA CIMETIDINA EN LA FARMACODINAMICA DE LA TEOFILINA EN EL ESTADO BASAL:** Lalonde R. *Chest* 83, Feb. 1983.

La teofilina se metaboliza en el hígado por procesos de alquilación e hidroxilación y menos del 10% de una dosis se excreta intacta en la orina. Grandes variaciones existen en el aclaramiento de la teofilina entre paciente y paciente a niveles séricos en exceso de 20 microg/ml. conlleva la presentación de síntomas desde leves como náuseas; hasta convulsiones y muerte súbita.

Algunos reportes en la literatura han sugerido que la cimetidina disminuye el aclaramiento de la warfarina, diazepam, chlórdiazepaxido y antipirina. Se cree que el mecanismo de interacción sea inhibición competitiva de las oxidasas a nivel de la microsoma de la célula hepática.

El estudio se diseñó para investigar los efectos de la cimetidina en la farmacodinámica de teofilina en condiciones basales luego de una dosis oral.

Los sujetos eran siete hombres con edad promedio de 28 años sin evidencia de enfermedad alguna.

La dosis usada fue de 200mg. de aminofilina oral cada 6 horas en un grupo y en la segunda fase los sujetos ingirieron 200mg. de aminofilina y 300mg. de cimetidina cada 6 horas por tres días.

Los resultados demostraron que los niveles séricos de teofilina eran más altos cuando los sujetos ingirieron cimetidina y aminofilina que cuando ingirieron aminofilina solamente. El aclaramiento de teofilina disminuyó en un 29% luego de una semana de administración conjunta de cimetidina y aminofilina.

Los autores sugieren que sus observaciones son compatibles con una disminución en el metabolismo de la teofilina debido a una disminución en el aclaramiento intrínseco de la droga y nó en otros factores.

**Comentarios:** Como se maneja la dosis de teofilina administrada varía de persona a persona y existen mayores variaciones en los pacientes en que usualmente la reciben como los asmáticos, enfisematosos, personas con fallo cardíaco crónico, así como gran variación debido a edad, peso, sexo y estatura.

Todo aquel que en el cuidado de sus pacientes incluya el uso de la teofilina y sus derivados debe de usar este artículo como un recordatorio de que la aminofilina como la digoxina siempre es mejor de menos que en exceso y a utilizar con frecuencia la determinación de los niveles séricos de la droga. Cimetidina es una substancia que no debe de ser usada como rutina en aquellos pacientes que estén recibiendo aminofilina y esteroides para el tratamiento de broncoespasmos. Es en vista de este artículo y de otro, (N.E.J.M. 1981, 304:672) que se relacionan con el mismo tema que los antiácidos usuales deben de usarse preferentemente para combatir la hipersecreción gástrica debido a la teofilina.

Ramón E. Figueroa-Lebrón, M.D.

**A RANDOMIZED TRIAL COMPARING CIMETIDINE TO NASOGASTRIC SUCTION IN ACUTE PANCREATITIS.** Goff JS, Feinberg LE, and Bungge WR. *Dig Dis* 1982; 27:1085-88.

Los autores hicieron un estudio randomizado comparando cimetidina a succión nasogástrica en 95 pacientes que tuvieron 103 episodios de pancreatitis. Alcohol era la causa de pancreatitis en 86%. Los datos principales de este estudio fueron que: 1. No hubo diferencia entre los dos grupos para un número de parámetros como duración de dolor abdominal, ileus, fiebre, hiperamilasemia, o complicaciones de terapia. 2. Los pacientes que recibieron cimetidina tuvieron una hospitalización más corta (6.8 días versus 8.5 para el grupo de succión).



La ventaja de cimetidina sobre succión en este estudio fue mínima pero el uso de cimetidina fue bien tolerado. Cimetidina se discontinuó en dos pacientes —en uno por tener cambios mentales y en otro porque desarrolló ileus que necesitó succión. La succión se discontinuó en cuatro pacientes —en dos por molestia del tubo y en dos por sangramiento gastroenteral (el sangramiento fue leve y no necesitó transfusiones).

Angel Olazábal, M.D.

**ACETYLSALICYLIC ACID SUPPRESSES THE RENAL HEMODYNAMIC EFFECT AND REDUCES THE DIURETIC ACTION OF FUROSEMIDE IN CIRRHOSIS WITH ASCITES.** Planas R., Arroyo V, Reinola A, et al: *Gastroenterology* 1983, 84:247-52.

Este interesante estudio por el grupo de hepatólogos en Barcelona reporta el efecto de ácido acetilsalicílico (AAS) y furosemiada (F) en la función renal de cirróticos con ascitis y sin azotemia. Reportan que 1. la administración de AAs disminuyó el flujo plasmático renal y la filtración glomerular; 2. la administración de F aumentó el flujo plasmático renal (FPR) y la filtración glomerular (FG); 3. cuando AAS fue seguido en 10 minutos por F no hubo cambio en FPR o en FG. Por lo tanto, la administración de F previno los cambios en función renal que ocurrieron con AAS.

Los autores comentan sobre la importancia de prostaglandinas en la perfusión y función renal. Postulan que AAS produjo los cambios en FPR y en FG por inhibición de la producción de prostaglandina  $E_2$  en los riñones y que F preservó la función renal porque F estimula la producción de prostaglandina  $E_2$ . Los autores comentan que se necesitan hacer estudios para evaluar si es beneficioso el uso de F en cirróticos que usan agentes anti-inflamatorios no esteroideos.

Angel Olazábal, M.D.

**FACTORES DE RIESGO PARA INFECCIONES EN EL LUGAR OPERATORIO DESPUES DE HISTERECTOMIA ABDOMINAL O VAGINAL.** Shapiro, M., et al: *N. Engl. J. Med.* 307: 1661-1666, 1701-1702, 1982.

Los factores de riesgo para infecciones post-quirúrgicas después de histerectomías fueron estudiados. Los datos fueron coleccionados prospectivamente en 323 pacientes que recibieron una histerectomía vaginal y 1125 pacientes que recibieron una histerectomía abdominal en el Hospital de Damas de Boston entre febrero de 1976 y abril de 1978. Utilizando análisis de regresión logístico se encontró que los factores que se asocian con un riesgo más alto de infección en el lugar de la operación fueron: 1) prolongación en el tiempo de la operación, 2) ausencia de uso profiláctico de antibióticos, 3) edad joven, 4) paciente perteneciente a la clínica, 5) el procedimiento abdominal. Después del análisis de todas las variables, se encontró que los siguientes factores no aumentaban el valor predictivo de un riesgo más alto para infección: 1) obesidad, 2) diagnósticos pre-quirúrgicos funcionales o anatómicos, 3) diagnósticos post-quirúrgicos o patológicos, 4) estatus menopáusico, 5) estimado de pérdida de sangre, 6) cirugía por un

cirujano en particular. El aumento en el tiempo operatorio se asoció con un efecto disminuido de los antibióticos profilácticos, cuya función preventiva bajó de 80 por ciento a una hora a un nivel no medible en 3.3 horas.

Carlos H. Ramírez-Ronda, M.D.

**ESPERMICIDAS VAGINALES Y GONORREA.** Jick, H., et al: *JAMA* 248: 1619-1621, 1636-1637, 1982.

Todos los cultivos positivos para *Neisseria gonorrhoeae* recuperados entre diciembre de 1978 y diciembre de 1980, de mujeres nacidas entre los años 1940 y 1960 fueron identificados en una clínica de Seattle, Washington. Se determinó en este grupo las tasas de gonorrea para las que se utilizaron anticonceptivos orales, espermicidas vaginales y las que tuvieron esterilizaciones quirúrgicas. La tasa de riesgo para las que se utilizaron espermicidas vaginales comparados con los otros fue de 0.23. Cuando mujeres con cultivos positivos para *N. gonorrhoeae* se comparó con el de mujeres con cultivos negativos, la tasa de riesgo para las que utilizaron espermicidas vaginales fue de 0.13. Los espermicidas vaginales tienen un efecto protector en contra de la gonorrea.

Carlos H. Ramírez-Ronda, M.D.

**TRANSCUTANEOUS NERVE STIMULATION IN RHEUMATOID ARTHRITIS.** Kumar V N, Redford J B: *Arch Phys Med Rehabil*, 63:595 - 596, 1982.

Este estudio de los efectos de estimulación (de nervios) transcutánea (TNS) en 20 articulaciones de la muñeca de once varones con artritis reumatoidea fue diseñado para hacer una evaluación objetiva del dolor y para evaluar los efectos de placebo del tratamiento. Después de determinar el tiempo que cada muñeca podía soportar un pequeño peso antes de que el dolor comenzara o aumentara (tiempo de carga) una prueba de tres partes fue llevada a cabo usando el mismo peso en cada caso. 1. Cada muñeca fue tratada con estimulación transcutánea (TNS) por espacio de 15 minutos y luego con el estimulador todavía encendido y conectado, el tiempo de carga fue obtenido (TNS-1). 2. Con el estimulador trabajando en la misma muñeca como en el grupo 1 (TNS-1), el tiempo de carga de la muñeca opuesta fue obtenido (TNS-2). 3. Para estudiar el efecto de placebo, el tiempo de carga fue obtenido con los mismos ajustes en el estimulador pero con la batería removida (TNS-3). Si el tiempo de carga aumentaba al doble o más, el alivio del dolor se consideraba 100%.

De los resultados se desprende que el 70% de las muñecas en el grupo 1 (TNS-1) tuvo una mejoría del dolor de 50 a 100%; 10% del grupo 2 (TNS-2) y 15% del grupo 3 (TNS-3) tuvieron alguna mejoría. Estimulación (de nervios) transcutánea reduce el dolor articular y ofrece un suplemento al uso de drogas antiinflamatoria.

Moises Santiago Vassallo, M.D.

**MEDIAN NERVE ANATOMY AND ENTRAPMENT SYNDROMES: REVIEW.** Wertsch JJ, Melvin J: Arch Phys Med Rehabil; 63:623-627 (Dec.) 82.

Los clínicos comunmente observan los signos y síntomas que resultan de atrapamiento del nervio mediano. Estos atrapamientos pueden ocurrir en sitios múltiples a lo largo del nervio. El nervio mediano se puede atrapar en la parte distal del húmero cuando el ligamento de Struthers, raramente presente, conecta una espuela osea del vástago del húmero al epicóndilo medial. El síndrome del pronador se refiere a compromiso del nervio mediano en la región proximal del antebrazo. El mismo puede resultar por atrapamiento del nervio entre las dos cabezas del pronador redondo, entre el pronador redondo y el flexor superficial de los dedos, o por la aponeurosis del tendón del biceps. La rama interosea anterior del nervio mediano está sujeta a compromiso cerca de su origen. Como nervio motor al ocurrir esto hay signos de debilidad muscular siguiendo el patrón del síndrome del nervio interoseo anterior. Este síndrome ocurre usualmente en forma espontánea pero puede ser causada por fracturas y bandas fibrosas. El tunel carpiano es un tunel fibro-oseo estrecho por el cual pasan nueve tendones. El síndrome del tunel carpiano es el más común de los atrapamientos del nervio mediano. Sus causas son muchas: cualquier factor que aumente el volumen de los contenidos del túnel o que disminuya el tamaño del tunel. Las anormalidades electrodiagnósticas existen más frecuentemente cuando este atrapamiento está presente que para otros atrapamientos del nervio. Variaciones anatómicas del nervio mediano ocurren frecuentemente y pueden traer confusión diagnóstica si no se reconocen. La certeza en el diagnóstico y el éxito en el tratamiento de los síndromes de atrapamiento del nervio mediano requieren el tener en mente los posibles sitios en que se pueden afectar el mismo: además de un conocimiento detallado de la anatomía pertinente.

**Moisés Santiago Vassallo, M.D.**



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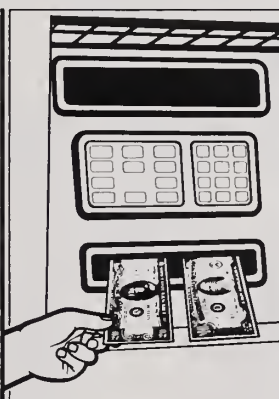
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Editado por: M.T. Press Ltd., Inglaterra, 1982

203 páginas, 12 capítulos

Tras la Primera Reunión Internacional de Glucagon en Gastroenterología, celebrada en Madrid, España, en 1979, de la cual surgió el primer volumen de esta serie<sup>1</sup>, y previamente reseñado en esta revista,<sup>2</sup> han tenido lugar una serie de adelantos clínicos y científicos que justificaron otro seminario de trabajo similar. En octubre de 1981, se celebró en Madrid, bajo los auspicios de la Universidad Complutense, la Segunda Reunión Internacional de Glucagon en Gastroenterología, coordinada por el Dr. Francesc Vilardell de la Escuela de Patología Digestiva de la Universidad Autónoma de Barcelona, con la participación de 14 investigadores, dos españoles y 12 extranjeros. La edición de los trabajos realizados fue llevada a cabo en forma extraordinaria, en el libro en epígrafe, por el Dr. J. Picazo.

La obra contiene los últimos adelantos en las distintas disciplinas y áreas adonde la hormona alfa-pancreática ejerce funciones fisiológicas, además de enfatizar su interés clínico y terapéutico.

El libro puede agruparse, artificiosamente, en tres secciones: una de implicaciones fisiofarmacológicas básicas del glucagon y sus análogos, una segunda de función gastrointestinal y sus implicaciones terapéuticas, y una tercera sección que nos presenta los conocimientos actuales del papel del glucagon y la insulina como factores hepatotróficos en el fallo hepático agudo.

Tras 60 años del descubrimiento del glucagon, éste se perfila no sólo como una hormona alfa-pancreática, reconociéndose su origen también a nivel gastrointestinal, constituyendo un factor importante en el metabolismo intermediario, contribuyendo al mantenimiento del metabolismo normal de adaptación a los estados de "stress" y trastornos metabólicos de múltiples procesos clínicos. Efectos farmacológicos insospechados del mismo, se han mostrado de utilidad con importantes aplicaciones clínicas prácticas y potenciales. Así, sobresalen su acción cardiotrópica, su capacidad regeneradora hepática o intestinal, sus acciones sobre la musculatura intestinal, biliar, y portales, sobre la secreción gástrica y el flujo biliar. Dichas acciones son evaluadas por distintos autores, al igual que sus efectos clínicos para estudios radiológicos y de terapia futura en pacientes afectados de estas áreas.

El glucagon pancreático es un inhibidor fisiológico de la secreción gástrica, tanto en el individuo normal como en los ulcerosos duodenales. Inhibe las constricciones gástricas pro-

ximales y distales, dando lugar a una reducción en el vaciamiento gástrico. Inhibe la presión del esfínter esofágico inferior, siendo su efecto farmacológico beneficioso muy conocido en pacientes acalásicos y con obstrucción esofágica alimenticia.

Su utilidad en el manejo de trastornos colónicos y cirugía colónica, al inhibir el espasmo y la motilidad intestinal, además de aumentar el flujo vascular intestinal, es poco conocida por los clínicos. Diversos estudios muestran la utilidad en el tratamiento de la diverticulitis aguda, en el tratamiento del sangrado por afección diverticulosa, en la obstrucción intestinal y el estreñimiento inducido por drogas. Su utilidad en estos, y en el manejo quirúrgico de procedimientos de anastomosis colónicas, de ileostomía post pan-proctocolectomía, en la intususcepción ileocólica, y en el diagnóstico diferencial de afección colónica aguda, son ampliamente documentadas en el capítulo desarrollado por O. Daniel de Inglaterra.

Su efecto espasmolítico en el esfínter de Odi es documentado por J.F. Rey y colaboradores de Francia, mostrando su utilidad en procesos que le afecten.

Hardcastle y colaboradores, de Inglaterra, presentan estudios clínicos mostrando su utilidad en el cólico biliar, y en los desordenes espásticos del esófago, intestino grueso y delgado.

Los capítulos de Okuda, y de Oka y colaboradores, de Japón, resaltan la clínica, fisiopatología, y los efectos clínicos del glucagon en el tratamiento del fallo hepático fulminante agudo. Butcher y colaboradores, de los Estados Unidos, muestran estudios en animales sobre el papel regenerador hepático del glucagón, que apoya su empleo terapéutico en pacientes con afectación de este noble órgano, como se resalta aún más con los trabajos de A.L. Baker, de Estados Unidos, en el tratamiento de pacientes con hepatitis alcohólica.

Al final de cada capítulo hay una sección de discusión con preguntas y respuestas muy pertinentes a los participantes y ponentes, que resultan muy útiles a las interrogantes que se le pueden plantear al lector. Esta forma de edición del libro lo hace muy útil, tanto para el clínico como para el investigador, permitiendo profundizar más en los trabajos y trayendo nuevas interrogantes.

Conjeturamos que con el desarrollo de las aplicaciones clínicas de glucagon, nuevas reuniones, al respecto, serán organizadas. Confiamos en el éxito científico de las mismas, al ser organizadas por el brillante hepatólogo Dr. J. Picazo, de quien conocemos su amplia preparación e inquietudes. Le felicitamos por la edición de este nuevo libro, el cual debe ser conocido por todo clínico que se envuelva en el manejo y evaluación de procesos gastrointestinales.

Adolfo Pérez-Comas, M.D., Ph.D.  
María T. Martínez de Prado, Lic. Farm.

1. Glucagon in Gastroenterology, Ed. J. Picazo, M.D., MTP Press Ltd., Lancaster, Inglaterra, 1979.

2. Pérez-Comas, A., Revisión de Textos Nuevos: Glucagon in Gastroenterology, ed. J. Picazo, Bol. Asoc. Med. Puerto Rico 72: 137, 1980.



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# Medicolegal Decisions



## VERDICT TO MOTHER IN WRONGFUL BIRTH SUIT NOT INADEQUATE, COURT RULES

As an offset to an award to a mother for "wrongful birth," a jury was under a duty to take into account the special benefits inherent in the parent-child relationship, a California appellate court ruled.

The mother consulted a gynecologist with regard to a bilateral tubal ligation. After the operation, a pathology report stated that a specimen submitted as a section of the left fallopian tube could not be identified as such.

The mother became pregnant about a year and a half later. The physician who examined her, a nephew of the gynecologist, offered to perform an abortion free of charge, arrange for adoption of the expected child, or perform another tubal ligation without charge. The mother decided to keep the child.

The mother sued the gynecologist, charging negligence in performance of the tubal ligation. There was a conflict in the expert testimony as to whether or not a surgeon performing a tubal ligation had a duty to ascertain the results of the postoperative pathologic examination and inform the patient. The gynecologist did not recall seeing the mother's report until after her pregnancy was confirmed, although the second physician found it in her file when he examined her. The jury decided for the mother and awarded her \$1,708 in damages.

On appeal, the mother contended that the damages awarded were inadequate. She contended that the value of probable expenses for raising her child to age 18 was approximately \$80,000, that her lost earnings were approximately \$5,000, and the value of a college education for the child was approximately \$10,000. She also contended that the trial court erred in permitting testimony as to her refusal to obtain an abortion or place her child for adoption to be received in evidence to establish a failure on her part to mitigate damages.

The appellate court said that although the latter evidence was objectionable on the issue of mitigation of damages, the mother could not assert it as a ground for reversal where it was first introduced on direct examination of the mother. She admitted that her child was beautiful, brought her more pleasure than pain, and had enhanced her relationship with the child's father. The court found that under its instructions, the

jury had a duty to take into account the benefits of the parent-child relationship, and that it could not be said as a matter of law that the award was outrageously inadequate or the trial judge erred in upholding it. Finding no abuse of discretion, the court affirmed the lower court's judgment.—*Morris v. Frudenberg*, 185 Cal.Rptr. 76 (Cal.Ct.of App., Aug. 16, 1982).

## DAMAGES LIMITED TO CERTAIN EXPENSES IN WRONGFUL BIRTH SUIT

A trial court erred in limiting the amount of damages for a pregnancy resulting from a physician's negligence to the expenses of delivering a child, the Alabama Supreme Court ruled.

A patient consulted a physician, complaining of cramps and abdominal bloating. At an exploratory operation, the physician found and removed cysts from the patient's fallopian tubes and ovaries. He dictated in an operative summary that the fallopian tubes were removed and allegedly told the patient that her tubes had been removed and that she was sterile. The patient later became pregnant and delivered a healthy child.

The patient sued the hospital and the physician, seeking compensatory damages for medical expenses and costs reasonably incurred in raising the child. After a pretrial hearing, the hospital settled for \$1,500, which was the amount of the patient's medical expenses. The trial court granted the physician's motion for summary judgment, finding that the patient could not recover more than the medical expenses.

On appeal, the court said that damages should be limited to the actual expenses and injury attending the pregnancy. The court said that such damages included physical pain, suffering, and mental anguish of the mother as a result of her pregnancy; the loss to the husband of the comfort, companionship, services, and consortium during the pregnancy and immediately after the birth, and the medical expenses incurred as a result of the pregnancy.

The court felt that any additional damages could have a significant impact on the stability of the family unit and the child, who would one day learn that he or she was not only not wanted by the parents but was raised by funds supplied by another person. The court held that there was no viable reason for exempting a physician from liability when his negligence caused a patient to become pregnant. Reversing the trial court, the appellate court sent the case back for further proceedings.—*Boone v. Mullendore*, 416 So. 2d 718 (Ala. Sup. Sup. Ct., June 30, 1982)



## MDS AND HOSPITAL LIABLE TO PATIENT

A verdict of \$1,000,000 against two physicians and a hospital should be affirmed, a Pennsylvania appellate court ruled.

A patient suffered neck and back injuries on July 13, 1964, in an automobile accident. He was hospitalized for eight days and then referred to two orthopedic surgeons. They treated him conservatively until December 31, 1964, when one of them performed a laminectomy with a discectomy and an interbody fusion between his third and fourth and fourth and fifth lumbar vertebrae.

Postoperatively, an infection developed at the operative site. Chloromycetin and neomycin were administered, but his condition continued to worsen. He had renal problems, hearing loss, and paraparesis. On January 26, 1965, an operation was performed to open and drain the infected wound and to remove the bones engrafted during the interbody fusion. He recovered and learned to walk with crutches, but he remained deaf.

In an action against the driver of the other automobile, the two orthopedic physicians and the hospital, the patient alleged negligent treatment. He claimed that the laminectomy was unnecessary, or that it should have been confined to the cervical area, that they should have opened and drained the wound sooner, and that they knowingly treated him with neomycin after learning of less toxic drugs to treat the infection. The physicians argued that the laminectomy was necessary to prevent paralysis, that it was proper to treat the infection with antibiotics before surgery, which would destroy the interbody fusion, and that their use of neomycin was in accordance with the drug's labeling.

A jury returned a verdict for the patient for \$10,000 against the driver and \$1,000,000 against the two physicians and the hospital. The appellate court affirmed the verdict, rejecting claims by the physicians that the trial court committed reversible errors.—*Pratt v. Stein*, 444 a.2d. 674 (Pa.Super.Ct., April 16, 1982)

## PATIENT'S SUIT AGAINST HOSPITAL NOT TOO LATE

A four-year statute of limitations applied in a malpractice action against a hospital that was a state agency, a Florida appellate court ruled.

A patient who became pregnant sued the hospital, alleging breach of contract and negligence in failure to perform a requested tubal ligation. The patient's complaint alleged that the matter had been submitted to a medical mediation panel.

The hospital contended that the two-year statute of limitations had expired before the suit was filed. It contended that it was an agency of the state and that the patient had not complied with the notice requirements under the waiver of sovereign immunity act. The trial court entered summary judgment for the hospital.

On appeal, the court found that the statute of limitations for a state agency was four years from the date the incident occurred. Where less than four years had elapsed between either the date on which the tubal ligation was to have been performed or the date on which such failure was discovered

and the date on which the complaint was filed, the court found that summary judgment was improper.

As to the allegation regarding the notice requirements, the court said that a written demand for medical mediation was served on the hospital, containing a detailed statement of the nature of the claim, how and when it allegedly occurred, and the damage claimed. The hospital responded to the demand by filing a written denial of the claim. The court found that the law did not specify the form or manner of submitting the claim except that it be in writing. Reversing the summary judgment, the court sent the case back for further proceedings.—*Whitney v. Marion County Hospital Distric*, 416 So.2d 500 (Fla. Dist. Ct. of App., July 7, 1982)

## PARENT SUES FOR ALLEGED NEGLIGENCE IN FAILURE TO PERFORM AMNIOCENTESIS

Summary judgment was precluded where there was an issue as to when parents learned that the birth of a Down's syndrome child could be predicted by amniocentesis, a California appellate court ruled.

A suit for prenatal malpractice was brought by a mother for her 8-year-old child with Down's syndrome. The complaint charged a physician with careless diagnosis, examination, and treatment, particularly negligence for failure to diagnose the abnormality, advise of the condition, and recommend a therapeutic abortion to the parents. The mother alleged that she could have had a therapeutic abortion in another jurisdiction, although it was illegal at that time in her own area.

The physician contended that the suit was barred by the statute of limitations. He also contended that the cause of action depended on the allegation that he should have committed an illegal act in advising the mother to have an abortion. The trial court dismissed the suit.

On appeal, the court held that an attending physician was under a duty to test a middle-aged woman for Down's syndrome and to advise the parents of the results of the test. The court said that the decision with regard to seeking an abortion should be left to the parents.

The mother alleged that the statute of limitations did not begin to run until the parents retained counsel and first discovered the existence of a cause of action. The physician argued that the parents should have realized that they had a cause of action when the Down's syndrome was detected, which should have been when the infant was born.

The appellate court said that the parents did know that the infant was born with Down's syndrome but did not know that it could have been predicted by amniocentesis. The court said that while the medical test might be well known to a small sophisticated and educated portion of the nonmedical population, it could not be said that a reasonable person not trained in medicine should have known about it.

The court found that whether the parents should have realized that the infant's condition could have been predicted by amniocentesis was a question of fact and that the case should not have been dismissed on the basis of the statute of limitations. The court reversed the lower court's judgment

and directed that the mother be allowed to amend her complaint in accordance with the court's opinion.—*Call v. Kezirian*, 185 Cal.Rptr. 103 (Ca. Ct. of App., Aug. 18, 1982)

### PARENTS CAN RECOVER FOR UNSUCCESSFUL STERILIZATION

Parents could recover damages for additional medical and surgical care after an unsuccessful sterilization operation, a New York appellate court ruled.

The parents filed suit against the physician who performed the unsuccessful operation on the wife on January 12, 1979. The physician moved to dismiss the complaint except for the portions seeking recovery for damages for the operation itself and pain and suffering. A trial court granted the motion, and the parents appealed.

The appellate court said that the damages excluded by the trial court should have been included as damages. Additional medical and surgical care, including cost and expenses of prenatal and postnatal care, were incidental to the unsuccessful sterilization process and could be recovered in the action, the court said.—*Nolan v. Merecky*, 451 N.Y.S.2d 914 (N.Y.Sup.Ct., App.Div., June 3, 1982)

### CHILD LOSES WRONGFUL LIFE SUIT AGAINST PHYSICAL

A child could not, in his own right, recover expenses incident to care and treatment or his physical impairment on a wrongful life claim, a Texas appellate court ruled.

The mother of a child afflicted with Duchenne muscular dystrophy was again pregnant. She and her husband consulted a physician to determine whether a physician to determine whether the mother was a genetic carrier of the disease so that they could decide whether to terminate the pregnancy.

The physician, who was director of a clinic designated by the Muscular Dystrophy Association of America, examined the mother and found normal muscle test results and reflexes, electromyogram, and creatine phosphokinase test. On two other occasions, he again found normal test results.

The mother gave birth to a son. Two weeks before his third birthday, during a routine nursery school examination, a podiatrist noted tight heel cords bilaterally. He referred the child to a specialist in pediatric neurology, who found that the child had Duchene muscular dystrophy. According to the specialist, the disease only becomes detectable by a trained eye when a child gets older and exhibits a clumsiness not attributable to being two years of age or to learning to walk.

Nine months after receiving the diagnosis, the parents filed suit against the first physician and a hospital, alleging negligence in assuring the mother that she was not a carrier of the disease and that her risk of having an afflicted child was no greater than that of the general population. The court granted summary judgment for the physician and hospital.

On appeal, the parents challenged the two-year statute of limitations on constitutional grounds, alleging that it barred

their claims before they were or could have been aware that they had such claims. The court refused to consider their constitutional claims and said that the Supreme Court had ruled that the limitations period ran from the date of an occurrence.

The parents also contended that the trial court erred in denying the child's claim for wrongful life. The appellate court found that a child could not recover damages for having been born at all or for expenses related to his defect or deformity. The court affirmed the trial court's judgment.—*Nelson v. Krusen*, 635 S.W.2d 582 (Tex.Ct. of App., May 3, 1982; rehearing denied, June 17, 1982)

### SUIT FOR ALLEGED FAILURE TO INFORM OF HEREDITARY DISEASE FILED TOO LATE

An action based on a physician's failure to inform a patient of a hereditary disease was barred by the statute of limitations, a federal trial court in Kansas ruled.

The physician took care of the patient's father from June 1959, to February 1960, operating on him for cancer of the colon. Before a second operation was performed, it was found that he had extensive polyposis of the colon. He died in April 1960.

The physician saw the patient from may 1960, to December 1968. The patient gave birth to a son in February 1971. In June 1980, he was found to have multiple familial polyposis. The patient died in 1981.

The patient's husband brought an action for negligence, fraud, wrongful death, wrongful birth, and wrongful life against the physician. The action was based on the physician's failure to diagnose and treat the patient and inform her that her father died of a hereditary disease, from which she subsequently died.

The physician brought summary judgment, contending that the suit was barred by the statute of limitations. The court said that the limitation period did not commence until a negligent act became reasonably ascertainable to the injured party. However, such action could not be commenced more than four years beyond the time of the alleged negligent act. In the present case, the latest possible date of occurrence of negligence was December 1968, the last date on which the patient was examined by the physician. Therefore, the causes of action against the physician ere barred in December 1972.

Since claims brought on behalf of the patient's child depended on allegations of negligence to the patient, his cause of action would be barred in December 1976.

The husband contended that the malpractice statute of limitation should not be applied to the other claims. The court pointed out that those claims arose from the failure to inform the patient of the hereditary disease. Where the latest date such failure could have occurred was 1968, the court found that the actions were barred. The court granted summary judgment for the physician.—*Brubaker v. Caranaugh*, 542 F.Supp. 944 (D.C., Kan., July 14, 1982)



## NO NEGLIGENCE IN BREECH DELIVERY

Two physicians were not negligent during a breech delivery, the Texas Supreme Court ruled.

The mother's physician, a general practitioner, worked unsuccessfully for about an hour trying to deliver the child. He called in an obstetrician, who performed an episiotomy and delivered the baby's legs, hips, torso, and arms. However, the child's head became lodged in the mother's pelvis. In order to aid delivery, he used Piper forceps to grasp the child's head. As he was pulling on them, the forceps slipped off the child's head. He reapplied the forceps and successfully delivered the child.

The child had indentations on both sides of his head. A pediatrician examined him and found no neurological damage. The indentations did not resolve themselves, and, when the child was about five weeks old, X-rays revealed bilateral fractures of the skull. A neurosurgeon operated and successfully elevated the fractures. The child fully recovered with no neurological impairment.

A jury found both physicians liable and awarded him \$2,000 for expenses and \$10,000 for pain and mental anguish. The two physicians were jointly liable for the \$10,000 and the obstetrician was solely liable for the \$2,000 award. An appellate court reversed the award against the obstetrician.

On further appeal, the Supreme Court said that neither physician was liable. The evidence did not support a finding that the physician was negligent in failing to inform the parents about a breech delivery. Although there was some evidence that the obstetrician breached the proper standard of care, there was no evidence that the breach caused the infant's injuries, the court said.—*Roark v. Allen*, 633 S.W.2d 804 (Tex. Sup.Ct., June 2, 1982; rehearing denied, June 30, 1982)

## MOTHER CAN RECOVER DAMAGES FOR BIRTH OF INJURED CHILD

A mother was entitled to recover for mental anguish suffered because of the birth of her child in an impaired condition, a federal appellate court in Texas ruled.

The mother was overdue when she was admitted to the hospital in labor at 10:30 p.m. Her physician was called, and he gave instructions but did not go to the hospital. When the mother's amniotic membrane ruptured, at 3 a.m., the hospital night supervisor called the physician and reported seeing green meconium. The physician called the hospital at 4 a.m. and ordered administration of a drug to stimulate labor. At 5 a.m., a nurse again called the physician, reporting other symptoms of fetal distress.

The physician did not go to the hospital until 7 a.m. Between 8 and 9 a.m., a nurse interrupted the physician during an operation on another patient, telling him of changes in fetal heartbeat. He finished the operation and then performed a cesarean section to deliver the child. The baby was transferred to a children's hospital, where a neonatologist found that there had been severe deprivation of oxygen and that the baby had permanent brain damage.

The mother brought an action for malpractice against

the physician. She claimed that he deviated from standards of sound medical practice in the delivery of her infant. The trial jury awarded \$1,600,000 for the child's medical expenses and \$175,000 for her lost future earnings and awarded the mother \$118,000 for mental suffering, which the court deleted.

The mother appealed the deletion of damages for mental suffering. The court said that under state law a bystander could recover to the extent that such injuries were foreseeable. The factors for determining foreseeability were location near the scene of an "accident," shock resulting from direct emotional impact from contemporaneous perception (as distinguished from learning of the accident from others), and whether the party was closely related to the victim.

The court said that not only was the mother located near the scene of the accident, she was in a sense the scene itself where the physician's negligence occurred to her and the child within her body. As a mother and child in childbirth, the relationship was unitary. As to the second factor, the court found that where the mother was conscious during more than 11 hours of painful labor and was aware of the physician's negligent acts, particularly his absence in a near-emergency situation and overadministration of a powerful drug, she had an experiential perception of the accident. The court found that she was entitled to compensation for the damages resulting from such suffering.—*Haught v. Maceluch*, 681 F.2d 291 (C.A.5, Tex., July 26, 1982)

## PHYSICIAN LOSES COUNTERSUIT

A physician's countersuit for physical and emotional damages was properly dismissed for failure to state a cause of action, a New York appellate court ruled.

A patient's widow had filed suit against the physician for allegedly causing the death of her husband. The medical malpractice action was dismissed on a summary judgment motion for failing to state a cause of action. The physician then filed a countersuit against the widow to recover for alleged physical and emotional damages resulting from the malpractice action. A trial court dismissed the complaint for failure to state a cause of action.

On appeal, the decision was affirmed. The complaint stated that the malpractice action was filed without reasonable evidence to support the claims of liability and damages. However, the trial court found that the physician was included in the malpractice action because his name was printed on two pages of an EKG report on the patient. That finding demonstrated that reasonable evidence existed to include him as a defendant.—*Drago v. Guonagurio*, 454 N.Y.S.2d 37 (N.Y. Sup.Ct., App.Div., July 15, 1982)

## PATIENT LOSES SUIT AGAINST HOSPITAL

A trial court did not abuse its discretion in refusing a motion to amend a complaint in a negligence suit after the statute of limitations had expired, a Pennsylvania appellate court ruled.

When a patient was being given a barium enema, the solution extravasated into the peritoneal cavity, causing severe pain. Emergency surgery was required.

In a negligence suit against the hospital, the patient's counsel was not able to proceed because his expert witness refused to testify. He cited his lack of expertise in the relevant area of medicine. A state medical society resolution provided for dismissal from the society of any member who testified for parties bringing malpractice suits in matters not in his or her area of expertise.

The patient submitted a report of a different expert, who stated that the extravasation was caused by perforation of the diverticulum but that he could not say with certainty whether the perforation occurred before or by means of the enema procedure. The report also stated that there was undue delay in diagnosis of and surgical correction of the extravasation.

The court denied the patient's motion to amend the complaint to include an additional allegation of negligence. Before jury selection, the patient presented another motion to amend, setting forth allegations of negligence in the hospital's failure to recognize and treat the barium extravasation, on the basis of the statement of the new expert witness. The motion was denied.

The trial court agreed with counsel for both parties that without the amendment the testimony could not sustain the original cause of action because the expert felt that there was no evidence that the enema tip had perforated the colon as in the original complaint. The trial court granted the hospital's motion for summary judgment.

On appeal, the patient contended that it was error to deny her motion to amend the complaint and to dismiss the complaint. The court said that while amendments were freely allowed, an amendment could not introduce a new cause of action after the statute of limitations had run. The limitation period had expired by the time the amendments were submitted in the present case. Finding that the motion to amend amounted to a new cause of action, the court found that the lower court correctly refused it. The court correctly refused it. The court affirmed the lower court's decision.—*Connor v. Allegheny General Hospital*, 446 A.2d 635 (Pa.Super.Ct., June 4, 1982)

#### VIABLE FETUS HAS RIGHT TO SUE FOR BRUTALITY

A viable fetus was a "person" within the meaning of the law and could bring an action to recover damages for alleged brutality, a federal trial court in Connecticut ruled.

A woman who was 5 1/2 months pregnant allegedly suffered severe and disabling head injuries as a result of being hit with a policeman's nightstick while another policeman stood by. She claimed that as a result of her head injuries her unborn baby also suffered serious physical injuries.

The woman brought an action against the policeman and the city on behalf of herself and her child, alleging that the policeman violated their civil and constitutional rights when he brutally struck her without cause or justification. She also claimed that the second policeman should be held equally responsible for the actions of the first because he failed to

restrain him. The policeman and the city moved for dismissal, claiming that a fetus was not a "person" within the meaning of the law and therefore could not recover damages.

The court said that recent and well-established trends in state courts have expanded the rights of the viable fetus in a wide variety of contexts, including injury by negligent operation of a motor vehicle, recovery for wrongful death by the estate of a viable fetus, and the definition of murder as killing a human being or a fetus. Therefore, the court denied the request to dismiss, finding that the fetus was a "person" under the law.—*Douglas v. Town of Hartford, Connecticut*, 542 F.Supp. 1267 (D.C., Conn., July 2, 1982)

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## American College of Physicians

### DR. DIAZ-RIVERA HONORED WITH MASTERSHIP IN ACP

Rurico A. Díaz-Rivera, MD, FACP, of Santurce, Puerto Rico was recognized for his outstanding contributions to medicine by the American College of Physicians (ACP). Dr. Díaz-Rivera and twelve other physicians were honored with ACP Mastership in the awards ceremony of the College's scientific meeting, in April 1983.

Dr. Díaz-Rivera, Director of the Department of Medicine at the Hospital De Diego, is a leading medical educator and expert investigator of inflammatory disease and heart disease. He plays an essential role in the founding and growth of the Medical School at the University of Puerto Rico and now serves as Honorary President of the Hospital De Diego staff.

A 1939 graduate of the University of Louisville, KY, Dr. Díaz-Rivera joins an elite group of his medical colleagues. Of the 54,000 ACP members only about 150 hold the rank of ACP Master.

Traditionally, Mastership is reserved for College Fellows such as Dr. Díaz-Rivera who have consistently upheld the highest standards of clinical performance and medical scholarship. These physicians have contributed other outstanding achievement to medical science as well.

Dr. Díaz-Rivera is now permitted to use the initials MACP after his name to signify the College's recognition of his accomplishments.

### USING ANIMALS IN RESEARCH IS NECESSARY BUT GUIDELINES ARE NEEDED

Using animals in research is essential for the advancement of medical knowledge, maintains the American College of Physicians (ACP). Still, investigators conducting research utilizing animals must perform these activities in facilities that meet appropriate standards to ensure the humane treatment, safety, and comfort of animals, the ACP asserts.

The College, which represents 54,000 doctors of internal medicine, related non-surgical specialists and physicians-in-training, issued its statement early this year. Certain areas of research require reliance on animal surrogates for human test subjects, the College notes, adding that the state-of-the-art of biomedical research has not, at this time, progressed beyond this point.

The College believes that a balanced approach will ensure the humane treatment of animals without unduly restricting the valid use of animals in controlled research settings.



## NATIONAL SOCIETY FOR MEDICAL RESEARCH

### ANIMAL RESEARCH VITAL IN ARTIFICIAL HEART SUCCESS

The University of Utah's success with the development of an artificial heart for a human was the result of experiments involving 250 animal implantations.

Three-month old calves were the best animals for this research because a human size heart would be too small for a full-grown cow and too large for most apes.

Because the calves would eventually outgrow the heart, the researchers also experimented with artificial hearts in full-grown sheep, taking special precautions during the operation due to the unusual sensitivity of sheep blood to the heart-lung machine that kept the anesthetized animal alive.

By late 1981 the laboratory had set a record by keeping a calf alive for 268 days before it succumbed to a mysterious infection.

Since that time a sheep has survived 7 months and is closing in on the record set by the calf. Five other living animals have had artificial hearts from 2 to 3 1/2 months.

### BARBITURATES CAN PREVENT LOWER BODY PARALYSIS

Barbiturates can prevent lower body paralysis when blood circulation to the spinal cord is temporarily blocked, according to a report from the Vanderbilt University Medical Center in the Journal of Neurosurgery.

Spinal cord damage resulting in permanent paralysis of the legs is a frequent complication when surgeon temporarily close the main artery supplying blood to the lower trunk and legs. Such surgery usually is done to correct aortic aneurysms and prevent a fatal rupture. Experiments with rabbits showed blood flow could be blocked for as long as 30 minutes with no damage when the animals were given barbiturates beforehand.

### HERPES DRUG REPORTED

A new drug being developed by the Upjohn Company has been found to prevent genital herpes infections in most mice and guinea pigs tested. Dr. Harold E. Renis reports the findings at the Interscience Conference on Antimicrobial Agents and Chemotherapy, which is sponsored by the American Society for Microbiology. The next step will be to test the drug in monkeys.



AMERICAN ASSOCIATION  
OF BLOOD BANKS

## NHF/ABRA RESPOND TO AIDS

The National Hemophilia Foundation's (NHF) Medical and Scientific Advisory Council, meeting in New York on January 14, formulated recommendations for manufacturers of factor VIII concentrate and cryoprecipitate with respect to Acquired Immune Deficiency Syndrome (AIDS). The recommendations call for efforts to exclude donors who might transmit AIDS through direct questioning of individuals belonging to high risk AIDS groups and evaluation and implementation, if verified, of surrogate laboratory testing.

Further, the recommendations call for the manufacturers of factor VIII concentrate to cease using plasma obtained from donor centers that draw from population groups in which there is a significant AIDS incidence and, referring to the geographic clustering of AIDS cases, state that "a great deal could be achieved by excluding donors from the 'hot spots.'" Concentrate manufacturers were directed to immediately cease purchase of recovered plasma for factor VIII concentrate from blood centers that do not make serious efforts to exclude donors through direct questioning concerning their belonging to a high risk group, and recommended that these criteria should also apply to the production of cryoprecipitate.

Other recommendations include the use of cryoprecipitate in the treatment of the following categories of patients unless there are overriding medical indications otherwise: 1) newborn infants and children under four; 2) newly identified patients never treated with factor VII concentrate; 3) patients with clinically mild hemophilia who require infrequent treatment. The potential advantages and disadvantages of cryoprecipitate or factor VIII concentrate for severe hemophilia A were seen as unclear and controversial at this time. No specific recommendations were offered concerning the use of cryoprecipitate or concentrate in this group, pending review of the data.

The American Blood Resources Association (ABRA), which represents most of the country's source plasma and plasmapheresis collection facilities, is recommending all donors be required to read informational documents which describe AIDS and that screening personnel ask those belonging to a high risk group (male homosexuals, recent residents of Haiti or intravenous drug abusers) to exclude themselves. In addition, ABRA recommends that prospective donors be asked directly whether or not they are a member of one of the high risk groups, and to exclude all those answering affirmatively. No large scale testing is being recommended at this time, pending the results of studies on economic impact, efficacy of tests, availability, etc. (These recommendations are pending Board approval).

ABRA is urging other blood banking groups to expand their questions to include similar screening procedures, stating that the joint recommendations from the voluntary sector don't go far enough.

In December, 1982, one of ABRA's members, Alpha Therapeutics, instituted screening and direct questioning of

donors, including the questions "have you ever used illicit drugs intravenously; have you ever resided in Haiti; or, to all male donors, have you ever had sexual contact with a man?" Alpha informed blood banks with whom it has contracts that it would not accept plasma from any center who did not institute such questioning.

## VOLUNTEER BLOOD BANKING SECTOR FORMULATES JOINT AGREEMENT ON AIDS

The American Association of Blood Banks, the American Red Cross and the Council of Community Blood Centers have formulated joint recommendations to address Acquired Immune Deficiency Syndrome (AIDS) as it relates to blood transfusions. AABB Institutional members were mailed copies of the joint recommendations on January 14. Any individual member who did not receive a copy should write to *News Briefs* at the National Office.

The deliberations which led to the joint recommendations brought unity to the three groups as they addressed a common problem which has been a major concern to blood bankers for the past several months.

Said Edward O. Carr, AABB president, "We hope that the type of cooperation which went into formulating this agreement can be repeated in the future. Reflecting on a past which has seen the emphasis placed on our differences, it was personally very satisfying to me to see the groups putting aside organizational differences and working toward a common goal."

The recommendations include a number of steps which can be taken by blood banks to address AIDS at the local level. These include extending educational campaigns to physicians regarding possible transfusion risks; more frequent consideration of autologous transfusion as an alternative to allogeneic transfusion, especially in elective surgery; preparation for increased requests for cryoprecipitate; expansion of donor screening to include specific questions to detect possible AIDS symptoms or exposure to patients with AIDS; not targeting specific donor recruitment efforts towards groups at high risk for AIDS; and working with the leadership of high risk groups.

The recommendations state that specific questions about a donor's sexual preference were inappropriate and ineffective in eliminating donors who may carry AIDS. While there is no specific test for AIDS, the recommendations note that there are laboratory and clinical findings that are present in nearly all AIDS patients, and the use of these nonspecific markers, for example, lymphopenia, immune complexes, and anti-HBc, are being evaluated in those areas of the country where AIDS is prevalent. (The major areas seem to be New York, San Francisco, and Los Angeles).

These recommendations were made on the basis of existing medical and scientific evidence. At the time of their formulation, only one AIDS case possibly related to transfusion had been confirmed by the Centers for Disease Control, and there have been fewer than 10 unconfirmed cases. There are approximately 10 million blood transfusions each year.

The joint recommendations grew out of a meeting of the AABB Committee on Transfusion-Transmitted Diseases, chaired by Joseph Bove, MD, which convened on January 6



to address AIDS. The meeting was expanded to include representatives from the American Red Cross, the Council of Community Blood Centers, The American Blood Commission, The National Gay Task Force, The National Hemophilia Foundation, The American Blood Resources Association, the Centers for Disease Control and the Food and Drug Administration.

### NEW ENGLAND JOURNAL OF MEDICINE REPORTS AIDS STUDIES

Two articles published in the January issue of *New England Journal of Medicine* address the possibility of AIDS being transmitted to patients with hemophilia through factor VIII infusion: "*Impaired Cell-Mediated Immunity in Patients with Classic Hemophilia*," by Michael M. Lederman, MD, Oscar Ratnoff, MD et al, and "*T-Lymphocyte Subpopulations in Patients with Classic Hemophilia Treated with Cryoprecipitate and Lyophilized Concentrates*," by Jay E. Menitove, MD, Richard H. Aster, MD, et al.

Both groups of researchers performed immunologic studies on healthy patients with hemophilia treated either with cryoprecipitate obtained from volunteer donors or with commercially prepared lyophilized factor VIII concentrates. The studies demonstrated that patients receiving lyophilized commercial factor VIII concentrates appear more likely to have abnormal T4/T8 ratios than those using single donor cryoprecipitate.

Both medical groups recommended caution in interpreting the meaning of their findings, however, since it is not known whether the abnormalities in the laboratory tests will prove to be persistent or transient, and studies of patients receiving larger amounts of cryoprecipitate will be needed to determine whether the AIDS-like picture is associated with commercial factor VIII only.

The Centers for Disease Control has reported similar findings in its studies of hemophilia patients with AIDS.

A related editorial in the *New England Journal of Medicine* concentrate and cryoprecipitate preparation, noting that concentrates are prepared from pooled plasma from 2000 to 5000 donors, while cryoprecipitate is prepared in the blood bank from the plasma of individual donors, with each bag finally containing about 100 units of factor VIII in a relatively small volume. The advantage of cryoprecipitable is that the recipient is exposed to only one donor per bag.

In the hemophiliacs studied, the difference between those receiving cryoprecipitate and those receiving concentrate does not seem to be explained by the fact that there was less treatment in the latter group, says Desforges, but one may wonder whether exposure to fewer donors is crucial.

Summarizing the freedom which concentrates have brought to the hemophiliac and the stress to blood banks providing sufficient quantities of cryoprecipitate, Desforges concludes "The present program has been extremely successful and would be given up by physicians and patients only with great reluctance. Yet is is time to consider doing so, even though we may not have enough evidence to demand such a radical change... Unfortunately, the data are consistent with a

greater potential for AIDS in the population treated with concentrate."



## AMERICAN COLLEGE OF SPORTS MEDICINE

### 1983 AMERICAN COLLEGE OF SPORTS MEDICINE ANNUAL MEETING

The world's largest professional and scientific society dealing with sports medicine announces their 30th Annual Meeting. The American College of Sports Medicine Annual Meeting will be held May 18-21 in Montreal, Quebec, Canada at the Queen Elizabeth Hotel.

One of the highlights of this four-day international meeting will be the J.B. Wolfe Memorial Lecture to be given by Dr. Frank R. Noyes from the Cincinnati Sportsmedicine and Orthopaedic Center, Inc. The title of his presentation is "Advances in the Understanding of Knee Ligament Instability, Repair and Rehabilitation."

The 1983 meeting will contain over 400 scientific papers to choose from. The enclosed outline lists the titles of the free communications sessions, symposia, colloquia, and tutorial lectures that will be presented. The sessions will feature such topics as: Eating Disorders, Exercise, and Sports Activities; Scientific and Clinical Aspects of Ice Hockey; Psychological Factors; Endorphins and Exercise; Body Composition; Preventive Medicine; Reproductive Hormones and Exercise; and many more.

Registration for the conference is \$90 for members and \$115 for non-members. A combined registration and ACSM membership package is available for \$150. Registration materials are available by writing to: ACSM, 1440 Monroe Street, Madison, WI 53706, or by calling (608) 262-3632.

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## ESTROGEN USE ASSOCIATED WITH LOWER DEATH RATES IN WOMEN

A possible protection effect conferred by naturally occurring estrogen in women has often been offered as a reason why women live longer than men. In a Feb. 1983 issue of JAMA, a group of researchers report that taking estrogen as a medication also appears to give users an advantage over nonusers in relative risk of death.

Investigators from five institutions studied the records of 2,269 white women aged 40 to 69 years who had been enrolled between 1971 and 1976 in the Lipid Research Clinics Prevalence Study of cardiovascular disease, according to primary author Trudy L. Bush, PhD, from the Oklahoma Medical Research Foundation, Oklahoma City. They examined the effect of estrogen use and nonuse on mortality rates in three groups of women: those who were gynecologically intact, those who had had the uterus removed, and those who had had the uterus and both ovaries removed. The women were followed up for an average of 5.6 years.

Bush and colleagues found that in all groups estrogen users had lower mortality rates than nonusers and that the strongest association between estrogen use and reduced risk of death was seen in women who had had the uterus and both ovaries removed. The association was weakest, although still significant, in women who were gynecologically intact.

The authors could not account for the higher risk of death in estrogen nonusers by differences in age, education, smoking habits, alcohol consumption, body mass, blood pressure or level of low-density lipoprotein cholesterol (LDL-C) in their blood [higher values of LDL-C have been associated with increased risk of heart disease]. They speculate that the apparent protective effect of estrogen use may be related to the ability of estrogen to raise blood levels of high-density lipoprotein cholesterol (HDL-C), higher values of which have been associated with a reduced risk of heart disease.

"In the present study, however," writes Bush, "HDL-C level accounted for some but not all of the lower risk of death in estrogen users. Another alternative explanation," she adds, "is that estrogen users have health-oriented behaviors that are different from those of nonusers and that may favorably influence mortality." This issue cannot be resolved from the study data, Bush says, nor can the dependence of lower death rates on the dosage or the duration of use of estrogen be assessed.

Because they cannot adequately explain their findings, "it would be premature to alter current estrogen prescribing practices," the researchers conclude.

## FIRST DES-LINKED CANCERS IN MEN

A 28 year-old man whose mother took diethylstilbestrol (DES) during pregnancy has developed testicular cancer. This is the first documented case of such cancer in males exposed to DES in utero, say a group of Boston physicians from Tufts-New England Medical Center in a March issue of JAMA.

According to Gene R. Conley, MD, Grannum R. Sant, MD, FRCS, Angelo A. Ucci, MD, and H. David Mitcheson, MD, diethylstilbestrol, a synthetic estrogen, was used widely in the United States from the early 1940's to 1971 to prevent spontaneous abortion and other pregnancy complications. "As many as 4 to 6 million mothers, daughters and sons were exposed to the drug," they write. "Subsequent findings of an increased incidence of clear cell adenocarcinoma of the vagina in the daughters and reports of doubtful efficacy of diethylstilbestrol for the prevention of pregnancy complications led to its discontinuation for that purpose in 1971."

Conley notes that multiple genital tract abnormalities have been reported in female and male offspring exposed to DES. In laboratory tests, adult male rodents exposed to DES in utero developed testicular tumors and renal tumors.

The authors offer three possible reasons for the fact that there have been no previous findings of testicular cancer in DES-exposed men. "First, patients with testicular tumors are not usually questioned about antenatal diethylstilbestrol exposure and, if questioned, may not know. Second, the peak incidence of seminoma (malignant tumor in testes) occurs in 30-year-olds, and since diethylstilbestrol exposure was most common in the 1950's, the group at greatest risk would be expected to be seen in the 1980's. Third, the association may not exist."

**Note:** Conley and colleagues add that they have since seen another case of seminoma in a 27-year-old man who was exposed in utero to DES. The young man also has five DES-exposed siblings, three of whom have genital tract abnormalities.

## DISEASE AND DRUG REACTIONS FOUND TO CAUSE MOST IMPOTENCE IN MEN

Contrary to the popular notion that male impotence is caused by emotional problems, disease or adverse reactions to medications were found to be the cause in 80 percent of impotent men who were evaluated in a recent Minneapolis study.

Michael F. Slag, MD, and colleagues from the Veterans Administration Medical Center and the University of Minnesota surveyed 1,180 middle-aged male outpatients of a general medical clinic. Of this group, 401 admitted to having a pro-

blem with impotence, and 188 of them agreed to be evaluated.

Fifty-five percent of the men evaluated had specific disease states that caused their impotence, including neurologic and urologic conditions, hormonal imbalances and diabetes mellitus. In 25 percent of the men, a medication was the likely cause of the impotence, with diuretics, antihypertensives and vasodilators most often implicated. Only 24 percent of the men had impotence attributable to psychiatric conditions. No specific cause could be found in seven percent.

The findings that 34 percent of the men in the survey were impotent demonstrates that this is a common problem among middle-aged and elderly patients with associated medical problems. Slag notes that only six of the 401 impotent men had previously had their problem identified; although most of the men evaluated were eager to discuss impotence with the investigators, they had been reluctant to call it to the attention of their own physicians.

The recognition of impotence is critical to good medical care of this population of men, the authors note. This is especially true of patients with drug-induced impotence who may, on their own, stop taking their medication and end up poorly treated. In addition, impotence places strains on sexual relationships that may lead to a decline in the men's self-esteem and self-care.

Slag advises a thorough medical evaluation of the impotent patient to rule out organic causes. A history and physical examination combined with a hormonal analysis should be the minimum. Such an evaluation can identify previously unrecognized disease or lead to changes in medication to reduce side effects. If those methods fail, Slag adds, the surgical implant of a penile prosthesis may allow the patient the potential to continue a satisfactory sexual relationship.

### USE OF ORAL CONTRACEPTIVES CLEARED OF CANCER RISK

Women with ovarian cancer are more likely to be younger than 30, never been married or pregnant, and have a diagnosed infertility problem.

Women with endometrial cancer (lining of the womb) are more likely to be older, white, obese, postmenopausal, and to have borne children.

Women with breast cancer are more likely to have had children, been older when their first child was born, have a history of breast cancer in first-degree relatives (mothers, sisters), and a history of benign breast disease.

Most significantly, no association appears to exist between the use of oral contraceptives and breast cancer. Furthermore, oral contraceptives appear to protect women against ovarian and endometrial cancer.

These are among the findings of extensive studies conducted by the Centers for Disease Control and reported in a March issue of JAMA.

Hailing the news in an accompanying editorial, Barbara S. Hulka, MD, MPH, says "The importance of these studies lies in their large sample size, the geographic diversity of subjects, the inclusion of cancer cases from each area (eight cancer registry areas were studied) and the randomly selected population-based controls."

Hulka points out that potential complications arising from the use of oral contraceptives have been studied intensively almost from the moment the substances were released to the public in the early 1960s. Cardiovascular complications were identified within eight years, and women over 35 were advised not to use oral contraceptives.

"However, the picture was not complete in the minds of many," Hulka says. "There lingered a concern that the steroid hormone composition of oral contraceptives would increase frequency of cancer after enough time had elapsed (15 to 20 years)." Now sufficient time has passed, Hulka says, "and for now the long-term news is good."

Not only were oral contraceptives cleared of suspicion with regard to the incidence of breast cancer, which affects 7% of American women sometime during their lives, they also were credited with lowering the incidence of endometrial and ovarian cancers, the third and fourth most prevalent cancers affecting women.

"This effect is expressed quantitatively by the population-based attributable risk that appears in the articles on ovarian and endometrial cancer," Hulka says. "The calculations provide an estimate of the number of cases in the U.S. population averted each year by oral contraceptive use. For 1982, 1,700 ovarian cancer cases and 2,000 endometrial cancer cases were averted."

The Centers for Disease Control studies were conducted by interagency agreement among the CDC, and the National Institute of Child Health and Human Development, and the National Cancer Institute.

The study on the long-term use of oral contraceptives and the risk of breast cancer involved analysis of 689 patients in eight cancer registry areas and 1,077 controls.

All women 20 to 54 years old with a first diagnosis of breast cancer were study subjects, and controls were selected at random from the general population within the eight study areas.

"Neither duration of oral contraceptive use nor time since first use altered a user's risk of breast cancer," CDC researchers say "Women whose first use was more than 15 years ago and who used oral contraceptives for 11 years or more had a relative risk of 0.8.

"Oral contraceptive use did not increase the risk of breast cancer among women with benign breast disease or a family history of breast cancer. Oral contraceptive use before a woman's first pregnancy did not increase her risk of breast cancer significantly more than other methods of delaying first pregnancy. This study provides no support to the hypothesis that oral contraceptive use increases a woman's risk of breast cancer."

The researchers were even more positive about the use of oral contraceptives in relation to the risk of ovarian cancer. From the eight cancer registry areas, 179 women aged 20 to 54 years with diagnosed ovarian cancer were enrolled in the study along with 1,642 controls...

The risk of ovarian cancer decreased with increasing duration of oral contraceptive use and remained low long after cessation of use. These results were not accounted for by parity, infertility, or other potentially confounding factors. We estimate that more than 1,700 cases of ovarian cancer (18,000 were diagnosed in 1982) are averted each year by past and current oral contraceptive use among women in the United States."



Similarly positive results came from the study of endometrial cancer. Again, women in eight cancer registry areas were enrolled in the study, including 187 between the ages of 20 and 54 years with diagnosed endometrial cancer and 1,320 controls.

"The protective effect occurred in women who had used combination oral contraceptives for at least 12 months, and it persisted for at least 10 years after the cessation of oral contraceptive use," the CDC researchers say. "The protective effect was most notable for nulliparous (child-bearing) women. These results were not accounted for by differences between cases and controls in health status, parity, infertility, or other potentially confounding variables.

"We estimate that approximately 2,000 cases of endometrial cancer (39,000 were diagnosed in 1982) are averted each year by past and current oral contraceptive use among women in the United States," the researchers conclude.

### INCIDENCE OF LIFE-THREATENING ECTOPIC PREGNANCIES SHOWN INCREASING

Both the numbers and incidence of ectopic pregnancies are on a dramatic upward spiral in the United States. Ectopic pregnancies occur when a fertilized ovum fails to reach the uterus, developing instead in the ovary, fallopian tube, or other extrauterine location, location, and creating potentially life-threatening conditions.

The number of ectopic pregnancies rose from 17,800 in 1970 to 42,000 in 1978, and the incidence more than doubled, from 4.5 per 1,000 to 9.4 during the same period, according to researchers from the Centers for Disease Control reporting in JAMA.

In Upstate New York, the rate of ectopic pregnancies per 1,000 conceptions increased by 217 percent from 1971 to 1979, say researchers from that state's department of health in a related Journal article.

The only bright spot in the reports is provided by the CDC observation that death rates from ectopic pregnancy declined by 75 percent during the study period, largely because of earlier detection and improved treatment.

The only bright spot in the reports is provided by the CDC observation that death rates from ectopic pregnancy declined by 75 percent during the study period, largely because of earlier detection and improved treatment.

The two reports "again emphasize the dramatic increase in the number of ectopic pregnancies that have been diagnosed during the past 10 to 20 years," comment David A. Eschenbach, MD, and Janet R. Daling, PhD, in an accompanying editorial.

"A twofold increase in the rate of ectopic pregnancy has been documented during the past 10-year period, and rates generally have been rising at an even faster pace during the past five years," they add. "This increase in ectopic rates has occurred among a wide variety of population in many industrial countries."

Eschenbach and Daling point out that the annual number of ectopic pregnancies in the US is now estimated at 40,000 and that such pregnancies still accounted for 5 percent of reproductive deaths both in 1955 and 1975. In addition to morbidity

and mortality problems, there is a 50 percent infertility rate after an ectopic pregnancy.

"Even then a pregnancy occurs, the chance of delivering a live-born infant is reduced," they say. "There is a 10 percent to 15 percent risk of a subsequent ectopic pregnancy in women who have had a prior ectopic pregnancy."

Acute salpingitis (pelvic inflammatory disease) appears to be a leading cause. "Women with documented acute salpingitis have an ectopic pregnancy rate that is increased sevenfold over women who have had no known salpingitis. Seven percent of the first pregnancies that occur after salpingitis are ectopic."

Other identified causes include gonorrhea, gravidity (number of pregnancies a woman has had), socioeconomic status, changes of contraceptive methods (most notably tubal ligation, intrauterine device, and low-dose progestational agents), and induced abortion, cesarean section, fertility induced by ovulatory drugs, pelvic surgery, and fetal diethylstilbestrol (DES) exposure.

To study trends of the occurrence of ectopic pregnancies, the CDC researchers examined two data sets from the National Center for Health Statistics: the National Hospital Discharge Survey; and the national vital statistics on mortality by cause.

They found that more than 260,000 women between the ages of 15 and 44 were discharged from US hospitals with a diagnosis of ectopic pregnancy from 1970 through 1978. Both the numbers and incidence more than doubled, and the overall incidence for the period was 7.1 per 1,000 reported pregnancies.

They also found that the risk of ectopic pregnancy increased with age, that it was greater for nonwhite women than white women, that a pregnant nonwhite woman at age 35 or greater had approximately a 2.6 percent chance that her pregnancy was ectopic, and that the death-to-case rates for ectopic pregnancies have declined, but the rates for nonwhite women have remained consistently higher than those for white women.

The New York State researchers analyzed ectopic pregnancies reported to the health department between 1971 and 1979 by maternal age, race, and gravidity. The rate per 1,000 conceptions increased by 217 percent during that period, they found, and learned that the percentage of increase was greater for women over 30, for white women, and for women with three or more previous pregnancies.

"These data supported those of others reporting an increase in the rates of ectopic pregnancies in recent years," the researchers comment. "The percentage increase differed by maternal age, race, and gravidity, being greatest among older women, white women, and women with higher gravidity."

Editorial observers Eschenbach and Daling call for further studies. "It seems possible that multiple factors have accounted for the increasing ectopic rates, including but not limited to an increased maternal age, increased salpingitis rate, changes in contraceptive practices, and an increase in early detection," they say.

"Well-designed studies using proper controls and multivariate statistical techniques will make it possible to quantitate more closely the importance of all the hypothesized factors in the future," they conclude.

## TOXIC SHOCK SYNDROME: ANYONE, ANYTIME

Realization is growing that staphylococcal toxic shock syndrome —associated almost idly in the public mind with tampons and menstruating women— can strike individuals of either sex at any age.

Adding to the body of knowledge about the disease is a report in a Feb. 1983 issue of *JAMA* about toxic shock syndrome occurring in a 30-year-old man. According to his physician, Jay A. Jacobson, MD, at LDS Hospital, Salt Lake City, the patient suffered all the effects characteristic of the disease —chills, fever, low blood pressure, muscle aches, a rash followed by peeling on his hands and feet, and abnormal functioning of his gastrointestinal system, heart, kidneys and liver. *Staphylococcus aureus* bacteria were cultured from lesions of herpes zoster ["shingles"] on the man's back.

Toxic shock syndrome is generally thought to be caused by a toxin produced by the bacteria. How the toxin evokes its effects is unclear, Jacobson says, but the toxin is probably a potent one because the total number of bacteria in his patient's skin lesions could not have been large.

Toxic shock Syndrome has been recognized as a disease since 1927, Arthur L. Reingold, MD, of the Centers for Disease Control (CDC), Atlanta, writes in an accompanying editorial. Many of the small number of cases reported before 1980 involved children. Since the widely publicized 1980 epidemic in menstruating women —and after the withdrawal of certain tampon products from the marketplace— the incidence of toxic shock syndrome has apparently declined.

It has become increasingly clear, however, that the disease can affect a wide variety of patients, Reingold says. About 15 percent of cases currently reported to the CDC involve surgical wound infections; infected burns, scratches and insect bites; septic abortion; postpartum infection; and a number of other conditions unrelated to menstruation and tampon use. The number of conditions and infections associated with toxic shock syndrome can be expected to increase, according to Reingold.

## MEDICINE ACCEPTING COMPUTER TECHNOLOGY BIT-BY-BIT

Information management is integral to the clinical practice of medicine, yet physicians are woefully slow in accepting new technologies that will help them manage today's rapidly expanding base of knowledge, according to a physician writing in a February 1983 issue of *JAMA*.

Daniel Levinson, MD, from the Department of Family and Community Medicine, University of Arizona College of Medicine, writes: "Computer and telecommunication technology has created an information management tool of enormous power and versatility. Practical, cost-effective systems for automated medical records, hospital management, decision making, drug information, electronic mail and message service, literature search and quality assurance protocols are

available now; more sophisticated ones, especially high-level artificial intelligence programs that closely imitate sophisticated diagnostic and therapeutic decision-making processes, are under development."

Levinson, astonished that "the medical profession, which generally welcomes new technology, has been so slow to recognize the clinical potential of computers," blames inertia, pride and lack of medical school leadership for what he calls "continued use of dangerously inadequate information-handling methods".

Levinson believes the most exciting developments are coming from innovative physicians who are discovering the clinical potential of an inexpensive personal computer. He points to the upsurge in attendance at a yearly symposium on computers in medicine, a number of computer-medicine specialty journals, and the recent inauguration of the AMA/GTE medical information network as an indication of growing interest.

Levinson does not believe that the human touch will be lost in computer-assisted medical practice, as some critics maintain. In fact, he says, "only when computers are assigned the laborious, time-consuming tasks of information management will the clinician be able to direct undivided interest and attention to the patient as a person... The computer can liberate the physician to exercise those uniquely human skills while at the same time placing complex diagnostic and therapeutic decisions on a far more accurate and scientific basis than is now the case."

Thomas L. Lincoln, MD, from the Los Angeles County/University of Southern California Medical Center, agrees in part with Levinson's assessment of why clinical medicine is slow to implement computer technology. However, Lincoln, writing in the same issue of *JAMA*, says that the products of computer science may still be too immature. He says that the products of computer science may still be too immature for widespread introduction into medical practice. "Physicians are willing to use any reliable and effective technology," he says. "Lack of clinical use indicates flaws in these products."

Lincoln cites rigid, business-oriented computer languages as part of the problem, since the uniqueness of medical applications calls for programming language flexible enough to handle the challenges posed by medical data. He also blames computer professionals who "have wrapped themselves in a private jargon and have underestimated medicine's understanding of its own information problems." Lincoln predicts a belated but rigorous growth for medical information science, aided by "the personal computer and the natural curiosity of a large cadre of health professionals and their teenage children."



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# CARDIO 83

## Asociación Puertorriqueña del Corazón

### SESION CIENTIFICA:

Seminario Sobre el Tratamiento en el Infarto Agudo del Miocardio  
y otros Temas Selectos.

3 al 5 de septiembre de 1983  
Hotel Palmas del Mar - Humacao, Puerto Rico

### CARDIO - 83

La Asociación Puertorriqueña del Corazón se complace en anunciar su Sesión Científica Anual CARDIO-83. Esta actividad científica tratará sobre el infarto agudo del miocardio. Se dictarán conferencias relacionadas con este tema, desde los factores de riesgo para el desarrollo de enfermedades cardiovasculares hasta la rehabilitación del paciente luego de sobrevivir un ataque cardiaco. Además se discutirán otros temas importantes tales como el seguimiento clínico del joven adulto con enfermedad congénita del corazón, el "stress" y las enfermedades cardiovasculares, adelantos y futuros desarrollos en las operaciones del corazón, incluyendo transplantes cardiacos y el corazón artificial.

### CREDITOS:

Esta actividad, co-auspiciada por la División de Educación Médica Continuada de la Escuela de Medicina UPR, y el Colegio de Profesionales de la Enfermería de P.R. se llevará a cabo en el Hotel Palmas del Mar en Humacao, los días 3, 4 y 5 de septiembre de 1983.

Los médicos recibirán (12) horas - crédito en Categoría I y los Profesionales de la Enfermería 15 horas contacto por C.P.E.P.R.

Próximamente recibirán el programa final, blancos de matrícula y registro del hotel.

Serán tres días de actualización intensa en Cardiología, tanto para médicos como para profesionales de la enfermería y personal aliado a la salud. Las conferencias se ofrecerán por las mañanas, dejando así medio día libre para actividades familiares, recreativas y para compartir entre amigos y colegas.

### INVITADOS:

Además de distinguidos conferenciantes locales, tendremos una facultad invitada compuesta por los siguientes profesionales:

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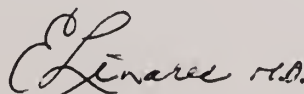
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Gracias al patrocinio de Medtronic, Inc., Marion Laboratories, Inc. y la Upjohn Inter-American, Corp., este evento cumbre de la Asociación Puertorriqueña del Corazón se ofrecerá a un costo módico. ¡Reserve estas fechas en su calendario!

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# ASOCIACION MEDICA DE PUERTO RICO

# BOLETIN

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuercen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

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El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquinilla a doble espacio; por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

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Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

### Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

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Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor. Debe indicarse en la parte superior de la ilustración.

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Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

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The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

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Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially.

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These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

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Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

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An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

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sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington, DC, May 3-7, 1971. 12. Pollak CP, McGregor PA, Weitzman ED: The effects of flurazepam on daytime sleep after acute sleep-wake cycle reversal. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, June 30-July 4, 1975. 13. Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

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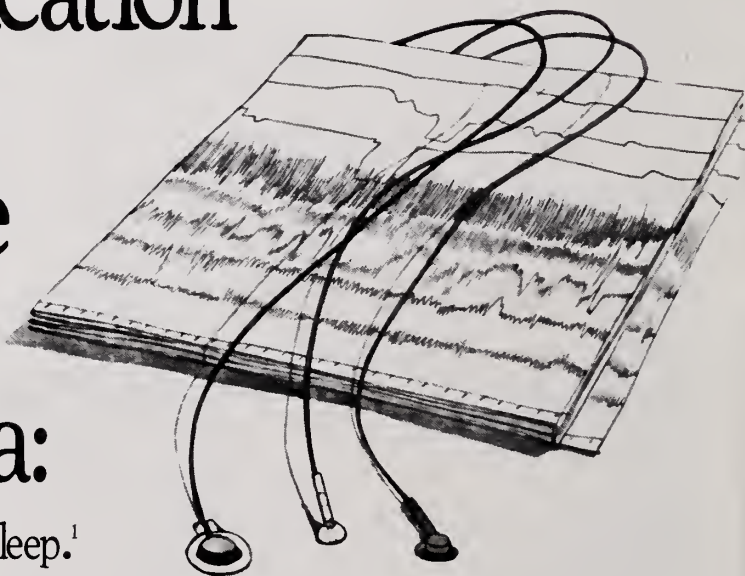
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BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO

PUERTO RICO



# BOLETIN

FRANCIS A. COUNTWAY  
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JUN 29 1983



VOL. 75 / NUM. 5

MAYO 1983





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Ave. Fernández Juncos Núm. 1305  
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Diego Román, Director Ejecutivo  
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Apartado 9387, Santurce, P.R. 00908

Publicación mensual, \$40.00 anuales. El Boletín se distribuye a todos los miembros de la Asociación Médica de Puerto Rico como parte de su cuota anual.

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USPS-060000

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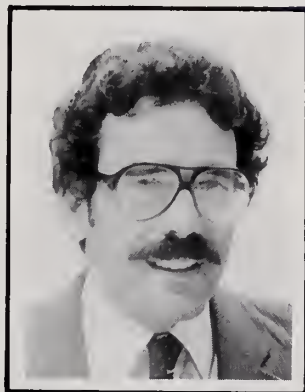
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# Columna del Editor



Nos complace comentar sobre este número ya que ha sido dedicado a la especialidad de Pediatría. Se ha diseñado con el Pediatra en mente y para ello hemos logrado conseguir la valiosa colaboración de prominentes sub-especialistas comentando sobre situaciones frecuentes en la práctica pero que aún son consideradas controversiales. La Sección de Autoevaluación es exclusivamente pediátrica y consta cada artículo de experiencias clínicas personales de sus autores.

Por primera vez aparecen fotografías a color en nuestra revista lo que sin duda mejora la calidad de los trabajos. Esto último ha sido posible gracias a donaciones de la Sección de Pediatría de la Asociación Médica y de la Fundación Médica de la Sociedad Española de Auxilio Mutuo y Beneficiencia.

La Junta Editora quiere también agradecer la colaboración de Mari Carmen Gómez hija del Presidente de la Sección de Pediatría, quien redactó "Nuestra Portada".

Nos sentimos muy satisfechos con este número pues aunque ha requerido esfuerzos mayores para su realización creemos que su contenido es de gran valor para todos aquellos que a diario trabajamos por preservar la salud y mejorar la calidad de vida de los niños puertorriqueños.

Queremos también dejar manifiesto que durante la preparación de este número especial siempre tuvimos mentalmente presente a nuestro antiguo Profesor de Pediatría, el Dr. Antonio Ortiz (QEPD). Sus enseñanzas y consejos han tenido una gran influencia en nuestra vida profesional. Por ello le estamos agradecidos, y estamos seguros que se sentiría satisfecho de este nuestro trabajo.

*Rafael Villavicencio*

Rafael Villavicencio, M.D.  
Presidente Junta Editora  
Boletín Asociación Médica de Puerto Rico  
Marzo 1983

ASOCIACIÓN MÉDICA DE PUERTO RICO

BOLETÍN



VOL. 75/NUM. 5

MAYO 1983

## NUESTRA PORTADA:

Niños en el Parque de las Palomas de David Goitia. El artista nació en San Juan en el año 1932. Desde joven mostró una especial afición por el arte, y careciendo de medios económicos para poder ingresar en una escuela de arte, asiste al taller de arte comercial del maestro Juan Rosado. Allí adquiere los primeros conocimientos en el arte del dibujo y la pintura y logra la oportunidad de conocer algunos de los principales artistas del país. Hacia el 1950 recibe el estímulo de Nino Sparacino, artista italiano que residía en Puerto Rico. Este lo entusiasma para que continuara sus estudios en Italia, pero su situación económica se lo impide. Conoce en este tiempo al artista español Carlos Marichal, quien toma al joven artista bajo su tutela y lo lleva como estudiante especial a su taller de artes gráficas en la Universidad de Puerto Rico. La influencia del maestro dejó una profunda huella en la formación artística de Goitia.

A fines de la década del '50, Goitia empieza a exponer en diversas galerías del país. En 1958 el Instituto de Cultura Puertorriqueña le otorga una beca para estudiar pintura mural y artes gráficas en México. Estudió bajo los maestros Cangiano, Ocampo y los hermanos Machado a la vez que trabaja como asistente del maestro González Camarena en la pintura de un mural. A su regreso a Puerto Rico, al siguiente año, expone su obra pictórica en la Galería Campeche e inicia su carrera como artista profesional.

Goitia es actualmente profesor de la Escuela de Artes Plásticas de Puerto Rico y ha expuesto sus grabados, serigrafías y pinturas en el Instituto de Cultura Puertorriqueña y en las principales galerías del país.

En los últimos años se ha destacado por sus carteles, producidos principalmente para el Instituto de Cultura Puertorriqueña.

En su serigrafía "Niños en el Parque de las Palomas", hecha para la Sección de Pediatría de la Asociación Médica de Puerto Rico en conmemoración de su Trigésimo Aniversario, el autor nos reproduce el hermoso Parque de las Palomas y aparecen esbozados un sinnúmero de simbolismos.

A un lado un anciano parece en total recogimiento y soledad al envolverse en su lectura, entre el cuchicheo sigiloso de los ingenuos niños al jugar.

Dos de los niños se presentan compartiendo sus inquietudes y admiración por una de las tantas bellas criaturas con las que Dios nos ha obsequiado. Mientras esto ocurre, un tercer niño solitario se encuentra envuelto en sus propios pensamientos y observa de forma indirecta, sin querer perturbar el juego de los niños con las blancas palomas.

Al fondo se puede apreciar la Capilla del Cristo, simbólico retazo de la influencia española en nuestra isla, la cual parece perpetuarse, a través de su sombra, en cada atardecer del Parque de las Palomas.

También aparecen preciosos arbustos que decoran este paisaje y que son símbolo de la bella vegetación que goza Borinquén.

Parece estar quieta la tarde..., sólo se escucha el arrullar de las palomas, y cada uno de los visitantes del Parque envuelto en su propio mundo; pero nuestro artista, en el envolvimiento de su arte, los recoge y al mirar al cielo disfraza en las nubes ese sentimiento de libertad que todo ser humano ansía.

Mari Carmen Gómez



## Mensaje del Presidente de la Sección de Pediatría

**E**l futuro de nuestra sociedad y la de todo el Universo está íntimamente ligado al bienestar de los niños. Por ello la Pediatría, desde sus comienzos, ha sido un baluarte de vanguardia en la profesión médica bregando con niños y sus padres para ayudar a alcanzar el máximo potencial de ellos como individuos y como familiares. Al desarrollar estos intereses y metas comunes, la labor del pediatra, en comparación con nuestros otros colegas, es admirable. La pediatría se convierte en una especialidad en la práctica de la medicina hace alrededor de un siglo, cuando se llegó a apreciar que los problemas de los niños son diferentes a los de los adultos y la prevalencia de esos problemas y la reacción de los niños a ellos varía con la edad. También nos encontramos con problemas de salud que varían no sólo de acuerdo a la edad, sino a muchos otros factores como son: raza, clima, geografía, niveles educacionales, económicos, socioculturales, respuesta del huésped a agentes nocivos, desórdenes genéticos, etc.

Los problemas contemporáneos en toda comunidad estimulan al estudio y a mejorar su manejo. Muchos problemas son reconocidos y llaman la atención del pediatra, levantando el interés por los trabajos de investigación. Todo ello trae como consecuencia el que ocurran cambios de gran importancia a través del tiempo con relación a la morbilidad y mortalidad en la edad pediátrica.

En las postrimerías del Siglo XIX teníamos en Estados Unidos que de cada mil recién nacidos vivos, morían doscientos de ellos antes de cumplir el primer año de vida como consecuencia de condiciones como: disentería, pulmonía, sarampión, difteria, tosferina y otros. Aquellos esfuerzos de los pioneros en el campo de la Pediatría, inmunología y salud pública llegaron al mejor entendimiento del origen y manejo de esos problemas haciendo que en la última mitad de este siglo la mortalidad infantil haya bajado de setenta y cinco por cada mil en 1925 a 15.2 en 1975<sup>1</sup>. Las tasas de mortalidad infantil en Puerto Rico revelan un cambio favorable de 43.7 muertes por cada mil en 1960, a 20.9 en 1977<sup>2</sup>, lo que nos coloca en tercer lugar en las Américas después de Canadá y Estados Unidos.

Estos logros en continuo desarrollo siguen a pasos agigantados gracias a múltiples factores, destacándose principalmente las maravillas del campo de la genética y bioquímica, nutrición, y el control de infecciones mediante inmunizaciones y nuevos y más efectivos antibióticos. Pero a pesar de todos estos adelantos que hacen u obligan al pediatra responsable a mantenerse al día en su lectura con una serie de materias mucho más variadas que cualquier otra especialidad, desde el conocer ochenta o más defectos congénitos que pueden ser diagnosticados por el estudio bioquímico y citológico del líquido amniótico, hasta las últimas recomendaciones en la nutrición del infante y el manejo de diferentes procesos infecciosos, existen otros factores que pueden lucir sencillos pero que también son de suma importancia ya que su falta menospreciaría grandemente el manejo del paciente pediátrico. La evaluación minuciosa de nuestros pacientes, la explicación cuidadosa a la madre y el manejo honrado de los diferentes problemas que se nos presentan a diario son fundamentales y necesarios siguiendo las pautas establecidas en la práctica de nuestra especialidad y con los logros adquiridos por los más recientes conocimientos a través de jornadas pediátricas o lecturas en diferentes revistas científicas. La limitación del espacio hace que no podamos discutir con más amplitud la importancia de estos últimos factores, pero podríamos citar varios ejemplos demostrativos que ayudarían a comprender mejor la importancia que estos tiene.

Las ansiedades de una joven madre lactante pueden ser grandemente aliviadas si le informásemos, por ejemplo, que el 48% del contenido del primer pecho y el 52% del segundo es consumido por el bebé en los primeros dos minutos de lactación; 89% y 80% a los cuatro minutos, y que por lo tanto, a los cuatro minutos, la ingesta de ambos pechos no varía significativamente del volumen ingerido en siete o diez minutos.<sup>3</sup> Que la insuficiencia de leche materna, manifestada por falta de distensión mamaria y crecimiento inadecuado del infante, además de dolor, ansiedad y fatiga por parte de la madre, se debe a la inhibición de la prolactina, lo cual puede eliminarse con la administración de chlorpromazina que actuaría remo-



viendo el factor inhibitorio.<sup>4</sup>

Otras veces pensamos que la madre no pueda lactar, no por producir insuficiente cantidad de leche, sino por causas mecánicas o pezones-areolas resentidas, y sin embargo, es debido al sabor de la leche secundario a un aumento en su contenido de sodio y cloro<sup>5</sup>.

A nivel de la utilización de agentes terapéuticos, podríamos también citar múltiples ejemplos. En el tratamiento de la sarna, el Hexacloruro de gamma benzeno no debe usarse durante el primer año de vida ya que su absorción transcutánea puede producir toxicidad significativa<sup>6</sup> y usar en su lugar crotamitón al 10% (Eurax).

Debemos cerciorarnos que la medicación por nosotros recetada sea a una dosis adecuada, que sea administrada como es debido, particularmente antibióticos y preparaciones de teofilina, y recordar que una "cucharadita" puede variar en su tamaño (de 4 a 7cc) y que es mejor usar algo más apropiado como un vasito medidor o jeringuilla para instruir adecuadamente a los padres.

Las infecciones en niños con enfermedades malignas siguen siendo la mayor causa de morbilidad y mortalidad, y aunque *E. Coli* y *P. Aeruginosa* continúan como prominentes agentes etiológicos, *S. Aureus* representa el 15-30% de las septicemias<sup>7</sup>, por lo cual el tratamiento inicial debe incluir una penicilina-penicilinas resistente o una cefalosporina más un aminoglicósido y carbenicilina (o ticarcilina) hasta obtener el agente causal y establecer el tratamiento específico.

El bajar la temperatura en niños es uno de nuestros problemas más comunes. Sabemos que el acetaminofen y la aspirina son igual de efectivos tanto por vía oral como rectal. También sabemos los efectos tóxicos de la aspirina, sobre todo en niños deshidratados. La dosis de acetaminofen de 10mg por kilogramo por dosis no ha sido efectiva en el manejo de la fiebre y por ello muchos han propuesto el uso alternado de aspirina y acetaminofen cada dos horas. La razón de esta terapia alternada es que ninguno de los dos antipiréticos alcanza niveles terapéuticos adecuados en las dosis usadas y por ello, debemos considerar el utilizar el acetaminofen en dosis inicial de 10-30mg por kilogramo seguido de 20mg por kilogramo por dosis cada tres a cuatro horas. Esto debe controlar la fiebre, el acetaminofen no se acumula, la toxicidad crónica no es un riesgo y niveles altos durante la deshidratación no ocurren, ya que se elimina por el hígado y no por el riñón.<sup>8</sup>

Mal uso y abuso de antibióticos... ¡Horrores! Nos erizamos cuando vemos tantos niños que llegan a nuestras oficinas con síndromes virales clásicos y tomando antibióticos. Ya hasta las madres, mayormente por culpa de los médicos, le piden al pediatra un antibiótico como si éste fuera un antipirético. Cuántas cefalosporinas son recetadas para otitis media sabiendo que no penetran al oído, además de ser otros los antibióticos de elección y más baratos. Cuántas diarreas por malabsorción o virales vemos recibiendo sulfa, ampicilina, neomicina o colimicina oral. ¡Horrores! En un estudio reciente<sup>9</sup> de un hospital pediátrico se encontraron errores en la administración de antibióticos en 30% de los casos médicos y 63% de los quirúrgicos. El error más frecuente fue el uso innecesario (13% en casos médicos y 46% en los quirúrgicos). Otros errores fueron en la selección del antibiótico, dosis, intervalos de dosis, vía de administración y duración del tratamiento. Un buen repaso del uso adecuado de los antibióticos puede encontrarlo en Mayo Clinic Proceedings, Enero, Febrero y Marzo, 1983 y Journal of Ped., Sept. '78 Vol. 93 (3).

Para mayor evidencia del uso inapropiado puede leer el estudio de Naqvi, J.A.M.A. 242: 1981.

Por último, no podemos terminar sin mencionar la gran cantidad de jarabes utilizados a diario, principalmente para el tratamiento de síntomas catarrales. Con gran frecuencia en nuestra práctica diaria nos encontramos con pacientes que llegan aquejando ciertos síntomas secundarios a jarabes recetados más bien siguiendo la promoción de un propagandista médico y, sin embargo, sin conocer básicamente lo que contiene el producto. El pediatra, o cualquier médico, no está obligado a saber manejar todos los productos que se encuentran en el mercado, pero sí es indispensable que aunque maneje pocos sepa lo que está recetando. Para ello le recomendamos ver el "medicinograma" que se encuentra en la página 236 y en el cual le dejamos espacio para que añada otros productos más utilizados por cada uno en particular.

Atendamos cada uno de nosotros nuestra conciencia para así lograr el mejor manejo de nuestros niños, su mejor bienestar y un futuro favorable.



M. Gómez Disdier, M.D., F.A.A.P.  
Presidente Sección de Pediatría  
Asociación Médica de Puerto Rico

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## Surgical Treatment of Congenital Heart Disease in Infancy: Why, When, What?

S. Subramanian, M.D., F.R.C.S.

The feasibility of surgical intervention in the symptomatic infant with congenital heart disease was established when Dr. Gross successfully performed ligation of the ductus arteriosus and Dr. Blalock performed the first subclavian-pulmonary artery shunt for cyanotic congenital cardiac disease. More recently, the feasibility of primary intracardiac repair in the infant at a risk comparable to or even superior to multiple stage procedures has been demonstrated and global results are uniformly good.

The frequency of cardiac malformation in the neonate does not seem to have changed in a 20 year period. Rowe and Mehrizi compared data obtained in two decades regarding frequency of cardiac malformations in the neonate (table 1). When the published series of 1965 is compared to the published series of 1975, there is virtually no difference with the exception of the persistent ductus arteriosus. This is easily explained on the basis of the increasing number of preterm

TABLE 1

Frequency of Cardiac Malformations in the Neonate		
	1965	1975
PDA	8%	31%
TGA	15%	12%
VSD	16%	11%
Hypoplastic left heart	9%	9%
Coarctation syndrome	8%	7%
T/F	8%	4%
Hypoplastic right heart	6%	4%
P V S	2%	3%
Others	28%	21%

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infants who are identified and treated aggressively in neonatological units in the country. There is, however, an interesting statistical information which has been made available more recently\* in that the overall incidence of congenital cardiac disease in the live newborn is not 6-8 percent per thousand births as was previously reported but is more in the order of 3.5 percent. It is clear, therefore, that the so called decrease in the incidence of symptomatic congenital cardiac disease in the neonate and the first year of life is due to two reasons: a) There is an absolute decrease in the birth rate and b) Previously assumed statistics are wrong.

About 50% of children with congenital heart disease will manifest symptoms in the first year of life and of these, only half need urgent surgical treatment for salvage. Classical examples would be hypoplastic left heart, coarctation syndrome and transposition of the great arteries. There are in addition to such moribund infants, a group of children in whom surgical treatment has to be offered in the absence of gross clinical symptoms to protect them from inoperability due to pulmonary vascular disease at a later age such as ventricular defect with pulmonary artery hypertension and common atrioventricular canal defect. In cyanotic infants, the ever present danger of cerebral thrombosis, embolism and infarction and abscess makes it mandatory that we should consider repair if it could be done at an acceptable risk.

A simple approach to the infant with cardiac disease would be to classify them as those that have: 1. obstructive lesions with shunts (valvular obstructions, coarctation of aorta, etc.), 2. increased pulmonary flow and heart failure (ventricular septal defect, atrioventricular canal defect, truncus arteriosus, etc.) and 3. decreased pulmonary blood flow and hypoxia (right to left shunt with pulmonary obstruction).

Table 2 and 3 lists the common cyanotic malformations and lesions which present in heart failure. There are other cardiac lesions such as left heart hypoplasia which are currently considered inoperable but increasing numbers of multistage procedures are being reported. Of the operable group, repair only is the treatment available for aortic stenosis, pulmonary stenosis and total anomalous pulmonary venous drainage whereas a choice between repair and palliation is available for other lesions such as transposition of the great arteries, tetralogy of Fallot and ventricular septal defect. There are some lesions for which palliative surgery is the only procedure currently possible. The objectives of surgical treatment of these infants resolves itself into three modalities:

- 1) to relieve obstruction,
- 2) normalize or reduce pulmonary blood flow either by repair or palliation (banding),
- 3) increase pulmonary blood flow either by repair or palliation (systemic to pulmonary shunt).

\* Ferencz, Scientific Exhibit, American College of Cardiology, 1983.



It is the purpose of this paper to discuss the why, when and what of surgical treatment of congenital heart disease in infants and also discuss the criteria for selection of patients for surgical treatment.

TABLE 2

Cardiac Malformations in Infancy: Cyanotic
T G A
T/F
Hypoplastic right heart
P.V.S.
Obstructed T A P V D
Complex

TABLE 3

Cardiac Malformations in Infancy: C.H.F.
PDA, AP window
Hypoplastic left heart
Coarctation Syndrome
VSD
AV Canal
Truncus
T A P V D
A.S.
Complex

Patent Ductus Arteriosus

Surgery for this condition has been available for nearly 50 years but more recently, the picture has been complicated by an increasing number of preterm infants who almost invariably have an associated persistent ductus arteriosus. We can therefore, discuss this lesion in two groups;

Group I — premature infants (a) in heart failure, (b) in respiratory distress. In the former, treatment is unquestionably the same as in the full term infants, namely try to control cardiac failure by medical means and if this should be unsuccessful, close the ductus arteriosus by surgical means. The intraoperative risk for surgical treatment of the ductus in the preterm infant is no different from that in full term babies. It is our practice to perform this procedure in infants over one kilogram in the surgical suite and in the nursery in the smaller infants. There have been no intraoperative deaths. In the latter group, the ductus arteriosus may be just an incidental lesion or aggravate respiratory distress. If echocardiogram shows a sizable left atrium which indicates an important left to right shunt through the ductus, surgical treatment is offered following an initial trial of aggressive medical management.

In full term infants, treatment is based on whether heart failure is controlled or uncontrolled. When heart failure is uncontrolled, surgery is immediate while in infants with controlled heart failure, the timing of surgery depends on the presence or absence of pulmonary artery hypertension. In the absence of pulmonary artery hypertension, these children can

be managed until they are older although there is no data to support the belief that surgery at a later date carries a lower risk since the risk is uniformly low in all ages. However, in the presence of pulmonary artery hypertension, it is imperative that early surgery be carried on to prevent pulmonary vascular disease. Finally, in full term infants with ductus arteriosus who are asymptomatic, the timing of surgical intervention is immaterial and we prefer to perform the procedure after six months of age since there is some evidence that even in full term infants, the ductus may close spontaneously up to six months after birth.

Coarction of the Aorta

Symptomatic isolated coarction of the aorta without ductus arteriosus or other anomalies is uncommon in infancy. However, preductal coarctation of the aorta is a serious condition and accounts for 22 of 56 infants under three months reviewed at our institution between 1966 and 1981. Four groups of patients were identified. (Table 4)

TABLE 4

Coarctation of the Aorta N = 56
I Isolated ± PDA = 22
II Coarctation + VSD = 16
III Coarctation + TGA ± VSD = 6
IV Coarctation + Complex anomalies = 12

The infant with ductus dependent coarction is precariously situated since concomitant with narrowing or closure of the ductus, the infants go into shock resulting in anuria, acidosis and death. Availability of prostaglandin E-1 has permitted the pediatric cardiologists to restore metabolic equilibrium to these patients and take them to the cardiac catheterization laboratory in an optimal condition to be followed by elective surgery. The surgical mortality statistics have ranged from an extreme of 100% down to 8% as seen in Table 5. Our own data includes patients in the pre-prostaglandin era and currently, in the absence of multiple complex anomalies, we do not encounter major problems in the surgical management of the isolated preductal coarctation of the aorta. A review of our data (Table 6) gives a breakdown of the four groups of patients in different age groups. The actual technique of repair of coarctation of the aorta in infancy is not of great debate currently. Most surgeons use the subclavian angioplasty technique. When the coarctation is complicated by large ventricular septal defect and pulmonary artery hypertension, there has been controversy regarding the management of the ventricular septal defect. Our preference has been to band the pulmonary artery concomitantly with coarctation repair. Fifteen out of 16 patients in this group underwent pulmonary artery banding. We have not regretted banding as an associated procedure except in two patients in both of whom the size of the ventricular septal defect was not outlined clearly prior to surgery and at autopsy, were found to be small. It is therefore, currently our practice to repair coarctation alone if the

initial study does not outline the ventricular septal defect clearly. The operative result in this group is comparable to the group without ventricular septal defect. In Groups III and IV, the mortality has been higher and it is related to the complexity of the associated malformations and it is our practice, (except in one who underwent Mustard operation) not to perform primary definitive intracardiac repair.

TABLE 5

Coarctation of the Aorta Published Mortality in Infants			
Reference	Year	Age	Surgical Mortality
Freundlich	1961	1 yr.	100
Chiariello	1976	3 mos.	57
MacManus	1977	3 mos.	32
Hermann	1978	3 mos.	44
Strafford	1980	5 mos.	8
Buffalo	1981	3 mos.	21.5

TABLE 6

Coarctation of the Aorta N = 56 Mortality					
	I	II	III	IV	Total
< 1 week	1 (0)	3 (1)	1 (0)	4 (4)	9 (5) 55.5%
1 wk — 4 wks.	12 (3)	5 (1)	4 (1)	—	21 (5) 22%
> 1 mo.	9 (0)	8 (0)	—	9 (2)	26 (2) 8%
Total	22 (3) 13.5%	16 (2) 12.5%	5 (1) 20%	13 (6) 46%	56 (12) 21.5%

( ) = deaths

### Ventricular Septal Defect

It is interesting to note that this relatively common and simple cardiac malformation has evoked such emotional response from cardiologists and surgeons since Muller and Damman proposed pulmonary artery banding to control blood flow in 1952.

Kirklin in 1961 proposed early intracardiac repair for isolated ventricular septal defect and documented satisfactory results. However, it was not until the early 1970's that repair of ventricular septal defect in infancy became routine. The earlier approach was to perform pulmonary artery banding as a preliminary procedure and perform total repair at the "optimal age" of four or five years. Analysis of our own data previously published showed that the banding operation was not a guaranteed preventive against pulmonary vascular obstructive disease. Additionally, a substantial number of chil-

dren after banding became cyanotic either due to acquired subpulmonic obstruction or outgrowth of the band. The second stage debanding and repair procedure carried a mortality around 10%. The two stage repair therefore, carries a salvage of less than 75%. Our data has shown that primary intracardiac repair of the symptomatic ventricular septal defect in infancy carries a mortality of less than 5% which is more acceptable than the staged procedure. It is unusual for infants with isolated ventricular septal defects to become very symptomatic in the first month of life. Usually, they are seen in follow-up at the pediatricians office when the neonatal pulmonary vascular resistance has dropped to normal resulting in increasing pulmonary flow and cardiac failure. Many of these children can be managed conservatively with medical treatment initially in the hospital and subsequently at home. The indications for surgical intervention in infants with ventricular septal defect in our hands would be failure of medical management, failure to thrive and feed necessitating repeated hospitalizations, and persistence of pulmonary artery hypertension at six months. The data from Kirklin (Figures 1, 2 3) shows that the overall surgical cure rate is related to the pulmonary vascular resistance. Those that have pulmonary vascular resistance of less than 4 units having the highest cure rate and

infants with pulmonary vascular resistance over 8, and certainly over 12 units, having the poorest cure rate. A cure is defined as normalization of right ventricular pressure without any residual sequelae of ventricular septal defect. Further analysis of the data shows that in the majority, complete cure can be achieved if the infant is operated before the age of one year. Unless there are specific contraindications, we believe that an infant with isolated ventricular septal defect who fulfills any of the three surgical criteria in the first year of life, should undergo primary intracardiac repair and not pulmonary artery banding. However, if the ventricular septal defect is multiple or complicated by other cardiac anomalies such as coarctation or transposition, we would not hesitate to recommend banding in very early life (< 3 months of age) and repair after restudy at about one year.



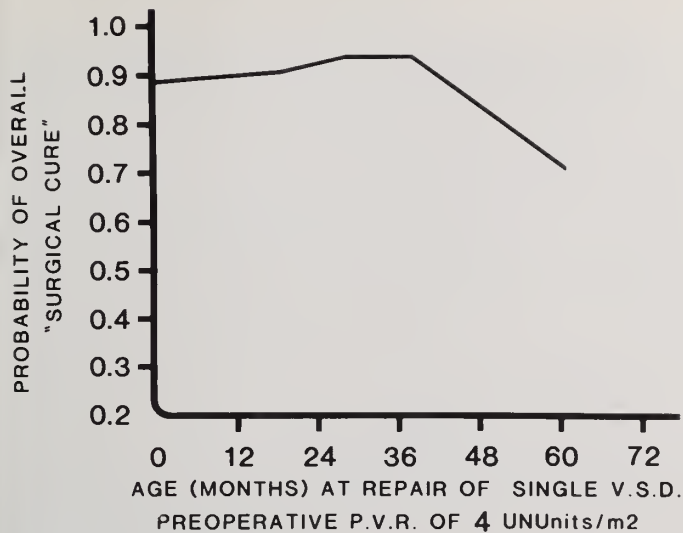


Figure 1  
Modified from Kirklin, et al, *J Thorac Cardiovasc Surg*; 1976, 72:661.

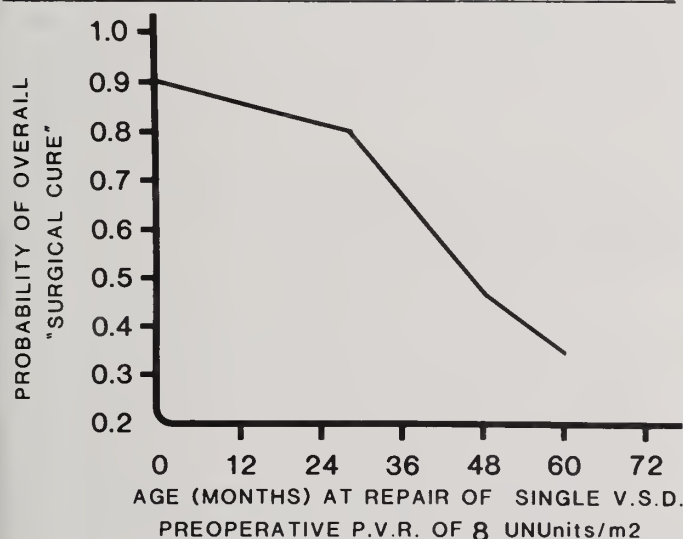


Figure 2  
Modified from Kirklin, et al, *J Thorac Cardiovasc Surg*; 1976, 72:661.

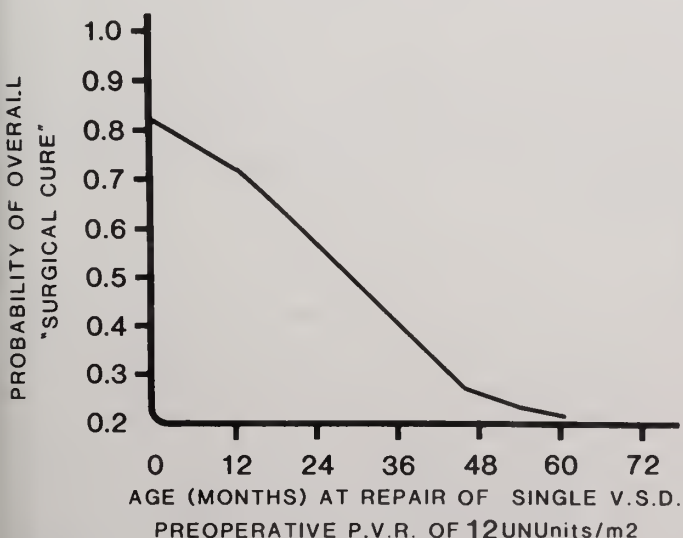


Figure 3  
Modified from Kirklin, et al, *J Thorac Cardiovasc Surg*; 1976, 72:661.

## Transposition of the Great Arteries

This lesion which is a lethal condition in the newborn has become more amenable to medical and surgical intervention over the last 15 years. Prior to the introduction of balloon atrial septostomy, the outlook for these children was grim. The majority died within the first month of life and only those with large natural atrial septal defect survived to one year. The infant with isolated transposition of the great arteries and intact ventricular septum was at greatest risk while the infant with ventricular septal defect and pulmonic stenosis in association tend to live longer as shown in a collective review by Leibman. Blalock Hanlon atrial septectomy carried a high surgical mortality since these children were extremely unstable metabolically and intraoperative deaths were common. The operative procedure itself required a great deal of surgical expertise. The introduction of balloon atrial septostomy was a stroke of genius in that at one procedure it was possible to confirm the diagnosis and carry out a therapeutic procedure which created a "medical" atrial septal defect. The defect allowed satisfactory mixing of the two circulations with improvement in the arterial saturation of the infant. Our early expectation that the balloon atrial septostomy would be a panacea and that these children would be allowed to grow to be three or four years of age was disillusioned when we reviewed our data and found that there was a gradual and progressive deterioration of arterial oxygen saturation between the age of three and six months. Examination of the size of the defect at surgery or at autopsy indicated that the defect was of adequate size in all and that any further attempt to increase the size of the defect surgically would not have contributed to an improvement in arterial oxygen saturation. In view of this, we reviewed our data and decided that with the availability of profound hypothermia and circulatory arrest, there was a place for primary intracardiac repair of transposed great arteries with intact ventricular septum electively between the ages of three and six months. This has been our policy since 1970 in children with intact ventricular septum. The urgency for reparative treatment in these children was also dictated by the fact that pulmonary vascular obstructive disease occurred even in the absence of a large ventricular communication; additionally these infants are at great risk to cerebrovascular accidents. Complicated transpositions with ventricular septal defect with or without outflow tract obstruction constitute a different problem. Our initial enthusiasm for open intracardiac repair extended to repairing these complex lesions early in life but the results were less than satisfactory. The best results in the group with ventricular septal defects were found when these children were operated in an elective condition after the age of six months. It is, therefore, our policy in this group to perform early pulmonary artery banding followed by repair before one year of age.

The surgical treatment of transposed great arteries and left ventricular outflow tract obstruction depends on the anatomy of the obstruction. Valvular and discrete subvalvular obstructions are easily treated whereas left ventricular tubular outflow obstruction does not lend itself to intracardiac repair and requires a valved external conduit. These patients are therefore, best treated by a systemic to pulmonary arterial shunt followed by a valved external conduit when they are about five years old.

Partial canal (ostium primum atrial septal defect) unusually presents problems in infancy. It is the infant with complete atrioventricular canal defect who presents in severe heart failure often uncontrollable by medical treatment. Even if controlled, they rapidly progress to pulmonary vascular obstructive disease. In view of this, these children have to be observed very closely clinically and by serial cardiac catheterization so that operative intervention can be timed before pulmonary vascular obstruction becomes excessive, ie. greater than six units. At cardiac catheterization, increased pulmonary vascular resistance is evaluated by hyperoxia and administration of prisolone. In the borderline case, an elective lung biopsy is performed, since in our experience, interpretation of frozen lung biopsy has not correlated well with fixed specimens. Although some children with atrioventricular canal defect have severe atrioventricular valve regurgitation, the majority of them have competent atrioventricular valve and it is therefore possible to consider them like a large ventricular septal defect and pulmonary artery hypertension. Pulmonary artery banding has been our election in the first three months of life when heart failure could not be controlled medically.

#### Total Anomalous Pulmonary Venous Return

The results of surgical treatment of total anomalous pulmonary venous return has improved considerably over the last five years. Much of this has been due to the availability of profound hypothermia and circulatory arrest, a better understanding of the techniques of intracardiac repair and the availability of prostaglandin to permit decompression of the ductus. The infant at greatest risk is the one with obstructed veins. These children present as an emergency and have to be stabilized and studied early and repaired. Profound hypothermia and circulatory arrest has been our method of choice to provide a bloodless operative field and a flaccid heart to permit careful anastomosis of the delicate structures.

The smallest such infant with infradiaphragmic drainage of total anomalous pulmonary venous return done at our institution was 4.4kg. The unobstructed total anomalous pulmonary venous return infant can be watched carefully since the problem here is of a large left to right shunt at atrial level. If, however, they should have pulmonary artery hypertension, even in the absence of pulmonary venous obstruction, we would recommend early intracardiac surgery. The determinants of success are shown in Table 7.

TABLE 7

Factors Determining Outcome in Total Anomalous Pulmonary Venous Connection
<ol style="list-style-type: none"> <li>1) Persistence of P A H</li> <li>2) Size of the left ventricle</li> <li>3) State of the left ventricle ie. endocardial fibroelastosis</li> <li>4) Size of anastomosis</li> </ol>

The hysterical enthusiasm for primary intracardiac repair of tetralogy of Fallot which was concurrent with the success achieved with correction of a variety of intracardiac diseases using profound hypothermia and cardiocirculatory arrest is now on the wane. It is now possible for us to look at tetralogy of Fallot objectively in terms of its pathology, operability, and long term results. There is no doubt that primary intracardiac repair can be achieved in selected patients but there is also no doubt that many patients who are unsuitable for primary repair are being subjected to this procedure when lower risk shunt operations are available. The major impetus for primary repair of tetralogy of Fallot in the early 1970's was the assumption that a shunt followed by definitive repair carried a much higher risk than a one stage procedure. This is no longer true. With the availability of Gore Tex grafts, systemic to pulmonary artery shunt has become a simplified procedure although the Blalock-Taussig operation contralateral to the aortic arch still remains the operation of choice in conditions which require augmentation of pulmonary blood flow. The indications for surgery are increasing cyanosis, polycythemia and hypercyanotic spells. When the anatomy is favorable consisting of adequate branch pulmonary arteries and absence of anomaly of coronary branching which would make outflow tract incision hazardous, it is our preference to do primary repair. When the anatomy is unfavorable, a systemic to pulmonary arterial shunt is done as described earlier. We have not yet followed the lead of Ebert and others in performing palliative outflow reconstruction in extreme variants of tetralogy and pseudotruncus.

#### Complex Cyanotic Conditions with Hypoxia

In other complex cyanotic conditions with oligemic lung fields and hypoxia, we continue to resort to palliative procedures such as Blalock-Taussig shunt or the modified Blalock-Taussig shunt using the Gore Tex tube. Extensive experience has been accumulated using Gore Tex tube shunts and the minimum acceptable size of tube in infancy is 5mm. The availability of prostaglandin E-1 has opened an entirely new field in newborn infants whose pulmonary circulation is ductus dependent. It has permitted the cardiologist to carry out invasive procedures on these infants electively and present a stable infant to his surgeon. With careful attention to detail which includes administration of prostaglandin E-1 during surgery, induced hypertension, avoidance of hypotensive anesthesia and systemic heparinization of the patient, the results of systemic to pulmonary surgical shunt have vastly improved.

#### Discussion

Fifteen years after the successful reintroduction of hypothermic circulatory arrest and universal enthusiasm over the availability of primary intracardiac repair in infants, we are now in a position to review with hindsight the appropriate method of surgical management of infants with congenital cardiac disease. Non longer is there any peer pressure to perform dramatic one stage procedures. Nor is there any need to delay repair by multiple staged palliative operations which introduces considerable emotional trauma to the family not to



mention the financial strain. We have attempted in this paper to lay out a plan of management of infants and discuss the why to operate, when to operate and what kind of procedure to offer.

The selection of patients for cardiac surgery depends on a multitude of factors. Patient selection depends on:

- 1) the unnatural history of the cardiac patient,
- 2) the symptomatology of the patient,
- 3) the anatomy of the condition and
- 4) the age and weight of the infant.

The selection of procedure however, could be either: a) palliation such as banding of the pulmonary artery, Blalock-Taussig shunt, etc. b) palliative repair such as palliative outflow reconstruction in pseudotruncus arteriosus, palliative external conduits, "primary repair" in tricuspid atresia and other complex malformations. In many of these cases, repair may be an anatomically accurate description but not necessarily a permanent one since these children require further procedures with growth. And finally, complete intracardiac repair is available in selective subgroups of patients at a low risk. This is classically exemplified in the excellent results obtained in the repair of ventricular septal defect, tetralogy of Fallot and transposed great arteries.

In order to assist the pediatric cardiologist and surgeon in the selection of patients for intracardiac surgery, there are certain determinants of selection of patients and procedures and this is based upon expectation of results. This includes the mortality statistics from the center, the morbidity of the procedure be it residual ventricular defect, heart block or pulmonary valve regurgitation and the expectation of a long term "cure". If anticipated results in terms of mortality and morbidity and long term cure are "acceptable", infants with symptomatic congenital cardiac disease should be offered intracardiac surgery. If, however, the anticipated long term cure by early repair is less than optimal, it is perhaps an advantage to stage the repair and wait for better procedures and greater expertise to be available with the passage of time.

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# Amígdalas, Adenoides y sus Problemas Alidados: Uso y Abuso de Tubos de Ventilación

Nelson Fernández-Blasini, M.D., F.A.C.S., F.I.C.S.

La cirugía de amígdalas y adenoides es la operación mayor, más comúnmente efectuada en los Estados Unidos y probablemente en Puerto Rico. Dicha operación equivale a cerca de la mitad de todas las operaciones mayores practicadas en niños, una cuarta parte de todas las admisiones a hospitales en niños y un 10% de días de hospitalización utilizadas por niños. En 1981 cerca de 766,000 procedimientos en amígdalas o adenoides fueron practicados en Estados Unidos, lo cual representa una reducción significativa del 1,103,000 de dichas operaciones practicadas en 1968.

Aunque el número de adenoidectomías sin tonsilectomía permaneció relativamente menor en comparación con el número de tonsilectomías bien sea practicada separada o en combinación con adenoidectomía, hubo un incremento en la práctica de adenoidectomía sin tonsilectomía.

El primer estudio fue hecho por el Dr. Albert Kaiser,<sup>1</sup> en el 1930, en Rochester, Nueva York.

## Indicaciones para la Tonsilectomía y Adenoidectomía

Considerables diferencias de opinión se han suscitado en la profesión médica en lo que concierne a las indicaciones para tonsilectomía y adenoidectomía. No existe mérito en estar clasificado en radical o conservador cuando un procedimiento quirúrgico está bajo consideración. La experiencia a través de los años nos convence de que los extremos se deben evitar y el operar o no operar debe ser determinado por los hechos y problemas presentados en cada caso individual. Todos los médicos con experiencia han visto resultados favorables y a veces "marcadamente favorable" luego de una tonsilectomía. Al igual, todos hemos visto casos en el cual el paciente no solamente no se ha beneficiado con la operación sino también ha empeorado de su condición inicial. Debemos tener en mente que la cirugía es una medida terapéutica de importancia. Por esta razón debe ser empleada con juicio clínico por excelencia.

La siguiente es una lista de condiciones para lo cual tonsilectomía y adenoidectomía ha sido recomendada:

TABLA I

Indicaciones para Tonsilectomía
1. Episodios repetidos de tonsilitis y adenoiditis (más de 5-7 por año), debidamente documentados.
2. Abscesos Peritonsilares (recurrentes).
3. Obstrucción mecánica en la deglución secundaria a hipertrofia marcada de amígdalas.
4. Crecimiento exagerado de una sola amígdala lo cual pueda enmascarar una enfermedad sistémica (ej.: linfoma, Hodgkin's, etc.)
5. Tonsilitis crónica (persistente por más de seis meses).

TABLA II

Indicaciones para Adenoidectomía
1. Cuatro o más episodios de otitis media "documentada", o otitis media serosa repetidas causando sordera de tipo de conducción.
2. Obstrucción de vía respiratoria por hipertrofia marcada de adenoides. (Pueden causar problemas secundarios como "Cor Pulmonare", etc.)
3. Problemas faciales o dentales y/o del habla relacionados con hipertrofia de adenoides.
4. Otitis media crónica, mastoiditis, alteración de la anatomía del oído medio, tumores de colesteatoma.
5. Sinusitis crónica, rinitis y nasofaringitis relacionadas con obstrucción adenoidea.

En la última década se ha discutido el valor relativo de cirugía de amígdalas y adenoides en la prevención de Otitis Media. La inflamación del oído medio u otitis media es la enfermedad más prevalente en la niñez luego de infecciones de vías respiratorias altas. Otitis Media con efusión (OME) puede ser aguda o crónica. OME aguda es usualmente de tipo supurativo, pero en algunos instantes se puede encontrar una efusión serosa en el oído medio. (Fig. 1). OME crónica tiene varios sinónimos, incluyendo serosa, secretoria, catarral, mucoide y sero-mucinoso ("glue ear"). (Fig. 2). Otitis media supurada crónica puede ser una secuela de OME aguda o crónica en cuya caso existe una perforación de la membrana timpánica o debida a un colesteatoma aural. La adenoidectomía practicada bien separada o en combinación con tonsilectomía es el procedimiento de cirugía mayor más frecuentemente empleado para prevenir estas varias formas de otitis media; la miringotomía con o sin la inserción de tubos de ventilación es el procedimiento quirúrgico menor más frecuente para OME.

A pesar de la alta frecuencia de su utilización, no se ha podido establecer mediante estudios científicos controlados el que los beneficios de cirugía de amígdalas y adenoides en otitis media exceden su costo en cualquier grupo de edad en niños.

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*Publicación Auspiciada por la Fundación Médica de la Sociedad Española de Auxilio Mutuo y Beneficiencia.*



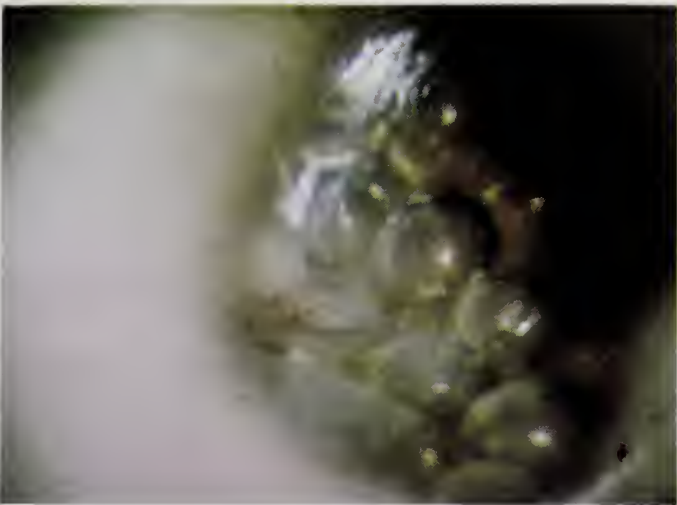


Fig. 1. Otitis Serosa (líquido en el oído medio.)

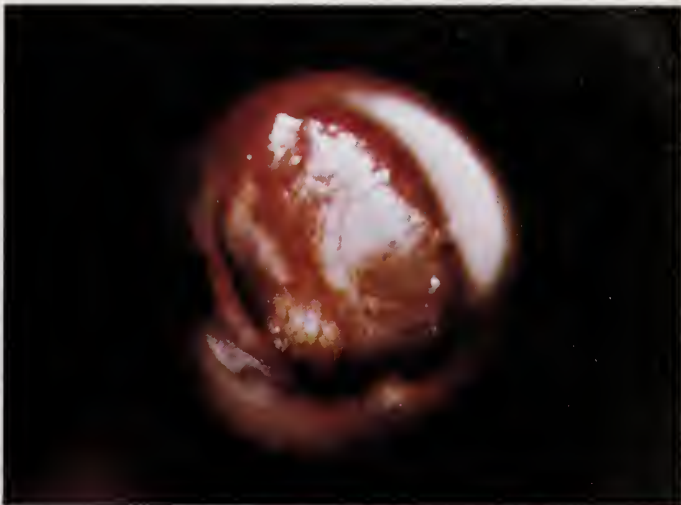


Fig. 2. Otitis Sero-Mucosa "Glue Ear".

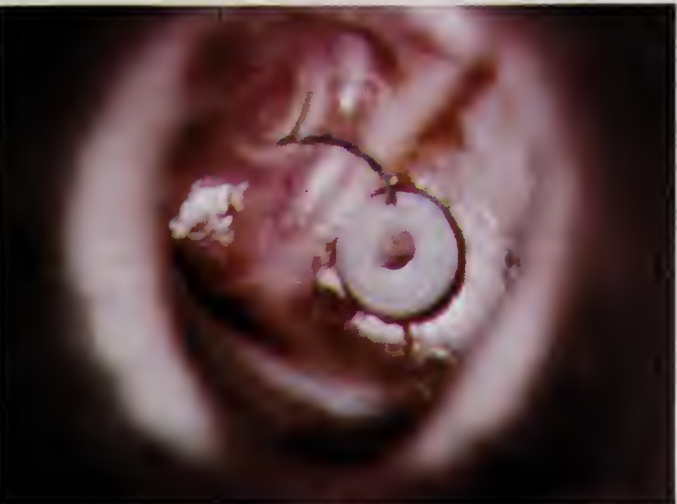


Fig. 3. Tubo de ventilación en la membrana timpánica.

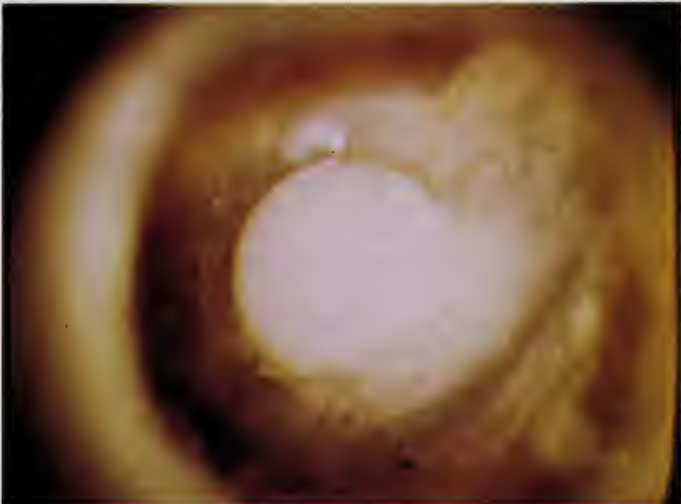


Fig. 4 y 5. Tumores de colesteatoma secundarios a perforación producida por tubos de ventilación.

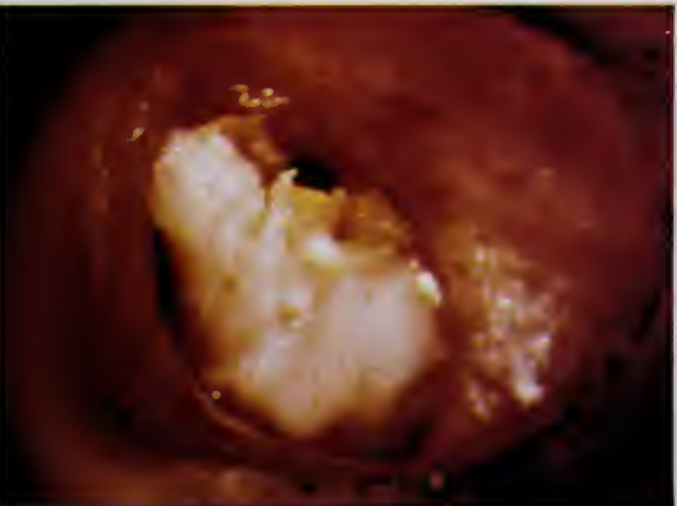


Figura 5.

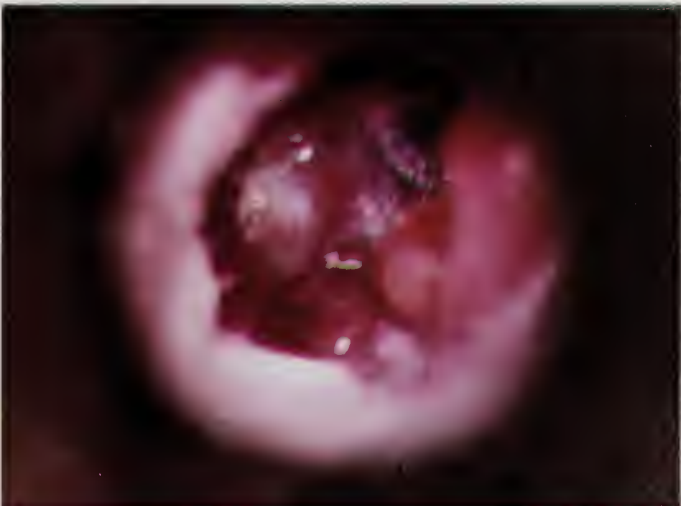


Fig. 6. Polipo secundario a perforación timpánica por tubo de ventilación.

Ha surgido interés en los últimos años en la función que juegan las amígdalas y adenoides en los mecanismos de defensa inmunológica del organismo. Las amígdalas parecen estar envueltas en la producción de linfocitos tipo B productores de globulina, e inmunidad celular por producción de linfocitos T.

En el Hospital de Niños de Pittsburgh, se lleva a cabo un estudio controlado para determinar la eficacia de Tonsilectomía y Adenoidectomía.<sup>2</sup> El efecto de adenoidectomía en OME es una de las preguntas principales en investigación, y uno de los criterios considerados en el estudio son episodios documentados de OME recurrente o persistente en un niño que ha tenido una miringotomía con inserción de tubo de ventilación por lo menos una vez anteriormente. Se debe efectuar una evaluación alérgica básica en cada examen individual.

El valor de la adenoidectomía en la prevención de OME permanece en una interrogante, pendiente de observación de una población mayor de niños en un período de tiempo mayor. No es obvio en el momento actual el que la adenoidectomía ofrezca alguna ventaja a todos los niños con OME por lo que hemos visto que luego de adenoidectomía no se elimina con certeza los episodios de OME.

### Uso y Abuso de Tubos de Ventilación

La inserción de tubos de ventilación (fig. 3) ha sido uno de los adelantos en el arsenal terapéutico del otólogo en el tratamiento de sorderas conductivas por OME en niños desde que Armstrong lo preconizó en 1954.<sup>4</sup> Tiene sus indicaciones precisas, pero desafortunadamente se abusa de su empleo.

Todo oído en niños debe ser inspeccionado bajo "microscopio operatorio" en el consultorio del Otorrinolaringólogo y no confiar simplemente en otoscopia con el otoscopio convencional.<sup>5 - 6</sup> Vemos frecuentemente niños que van a ser operados del oído para la inserción de tubos de ventilación porque se les practicó *timpanometría* y ésta registró una curva Tipo B y C sugestivo de líquido en el oído medio lo cual no fue confirmado clínicamente, otoscópicamente, ni en el acto operatorio haciendo miringotomía diagnóstica. El uso repetido de tubos de ventilación puede producir atrofia en el área de inserción con producción de una perforación permanente de la membrana timpánica y a veces con producción de tumores de colesteatoma, (Figs. 4 y 5) pólipos en oído medio (Fig. 6) y otitis media supurada con mastoiditis. Todo niño con tubo de ventilación debe ser examinado periódicamente hasta que el oído medio esté propiamente ventilado. De no haber extrusión del tubo, dicho tubo debe ser removido para evitar las complicaciones anteriormente descritas.

En el año 1975 se reportó un estudio practicado por los servicios quirúrgicos de los Estados Unidos indicando que menos de 40% de todas las tonsilectomías y adenoidectomías fueron practicas por Otolaringólogos Certificados (Diplomados por el Board Americano de Otolaringología.)

Es de práctica cada día más frecuente una "segunda opinión" por un especialista "Diplomado" para corroborar los hallazgos encontrados en la primera consulta.<sup>7</sup> De esta manera pueden obviarse procedimientos quirúrgicos que en vez de beneficiar al paciente hubiesen podido causar efectos secundarios adversos.

### Conclusiones

La tonsilectomía y/o adenoidectomía es uno de los procedimientos quirúrgicos más frecuentemente practicados en Puerto Rico y los Estados Unidos.

Una decisión a favor de tonsilectomía y/o adenoidectomía debe estar basada en un historial clínico cuidadoso, presencia definitiva de las indicaciones absolutas anteriormente descritas y una razonable "probabilidad de beneficio" para el paciente.

Se debe considerar por separado las indicaciones para tonsilectomía, adenoidectomía, y miringotomía con o sin inserción de tubos de ventilación.

Esperamos que en el futuro haya una mejor selección de pacientes, se realicen evaluaciones preoperatorias más consciencizadas y se mejore el seguimiento postoperatorio con un consecuente descenso en la morbilidad postoperatoria. En ninguna otra población de pacientes la doctrina de "primum non nocere" (primero, no cause daño); es mayormente aplicable.

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### FE DE ERRATA

Por error involuntario se omitió el nombre del Dr. Manuel Paniagua como co-autor del artículo Aspiración con Aguja Fina de los Nódulos Hipofuncionantes del Tiroides, publicado en el Vol. 5, Núm. 4, que corresponde al mes de abril de 1983.



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And what is more reassuring to an excessively anxious patient than medication that promptly starts to relieve his discomforting symptoms? Valium® (diazepam/Roche) begins working within 30 to 90 minutes. Patients continue to improve in just a few days, and relief continues throughout the course of treatment.

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Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Management of anxiety disorders, or short-term relief of symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic. Symptomatic relief of acute agitation, tremor, impending or acute delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in: relief of skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome. *Oral forms* may be used adjunctively in convulsive disorders, but not as sole therapy. *Injectable form* may also be used adjunctively in: status epilepticus; severe recurrent seizures; tetanus; anxiety, tension or acute stress reactions prior to endoscopic/surgical procedures; cardioversion.

The effectiveness of diazepam in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindications:** Tablets or capsules in children under 6 months of age; known hypersensitivity; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** As with most CNS-acting drugs, caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of predisposition to habituation/dependence.

**Use in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because their use is rarely a matter of urgency and because of increased risk of congenital malformations, as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**ORAL:** Advise patients against simultaneous ingestion of alcohol and other CNS depressants.

Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral forms adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may be associated with temporary increase in frequency and/or severity of seizures.

**INJECTABLE:** To reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling and, rarely, vascular impairment when used IV: inject slowly; taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer injectable Valium directly IV, it may be injected slowly through the infusion tubing as close as possible to the vein insertion.

Administer with extreme care to elderly, very ill, those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; concomitant use of barbiturates, alcohol or other CNS depressants increases depression with increased risk of apnea; have resuscitative facilities available. When used with narcotic analgesic eliminate or reduce narcotic dosage at least 1/3; administer in small increments. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs.

Has precipitated tonic status epilepticus in patients treated for petit mal status or petit mal variant status. Not recommended for OB use.

Efficacy/safety not established in neonates (age 30 days or less); prolonged CNS depression observed. In children, give slowly (up to 0.25 mg/kg over 3 minutes) to avoid apnea or prolonged somnolence; can be repeated after 15 to 30 minutes. If no relief after third administration, appropriate adjunctive therapy is recommended.

**Precautions:** If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of diazepam, i.e., phenothiazines, narcotics, barbiturates, MAO inhibitors and antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or over-sedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed and tolerated).

The clearance of diazepam and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

**INJECTABLE:** Although promptly controlled, seizures may return; readminister if necessary; not recommended for long-term maintenance therapy. Laryngospasm/increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic, have necessary countermeasures available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly/debilitated.

**Adverse Reactions:** Side effects most commonly reported were drowsiness, fatigue, ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity,

insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, discontinue drug.

Because of isolated reports of neutropenia and jaundice, periodic blood counts, liver function tests advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, observed in patients during and after diazepam therapy are of no known significance.

**INJECTABLE:** Venous thrombosis/phlebitis at injection site, hypoactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia. In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm/pain in throat or chest have been reported.

**Dosage:** Individualize for maximum beneficial effect.

**ORAL Adults:** Anxiety disorders, relief of symptoms of anxiety—Valium (diazepam/Roche) **tablets**, 2 to 10 mg b.i.d. to q.i.d.; or 1 or 2 Valrelease **capsules** (15 to 30 mg) daily. Acute alcohol withdrawal—**tablets**, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; or 2 **capsules** (30 mg) the first 24 hours, then 1 **capsule** (15 mg) daily as needed. Adjunctively in skeletal muscle spasm—**tablets**, 2 to 10 mg t.i.d. or q.i.d.; or 1 or 2 **capsules** (15 to 30 mg) once daily. Adjunctively in convulsive disorders—**tablets**, 2 to 10 mg b.i.d. to q.i.d.; or 1 or 2 **capsules** (15 to 30 mg) once daily.

**Geriatric or debilitated patients:** **Tablets**—2 to 2½ mg 1 or 2 times daily initially, increasing as needed and tolerated (see Precautions). **Capsules**—1 capsule (15 mg) daily when 5 mg oral Valium has been determined as the optimal daily dose.

**Children:** **Tablets**—1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use in children under 6 months). **Capsules**—1 capsule (15 mg) daily when 5 mg oral Valium has been determined as the optimal daily dose (not for use in children under 6 months).

**INJECTABLE:** Usual initial dose in older children and adults is 2 to 20 mg I.M. or I.V., depending on indication and severity. Larger doses may be required in some conditions (tetanus). In acute conditions injection may be repeated within 1 hour, although interval of 3 to 4 hours is usually satisfactory. Lower doses (usually 2 to 5 mg) with slow dosage increase for elderly or debilitated patients and when sedative drugs are added. (See Warnings and Adverse Reactions.)

For dosages in infants and children see below; have resuscitative facilities available.

**I.M. use:** by deep injection into the muscle.

**I.V. use:** inject slowly; take at least one minute for each 5 mg (1 ml) given. Do not use small veins, i.e., dorsum of hand or wrist. Use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute Valium with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer Valium directly I.V., it may be injected slowly through the infusion tubing as close as possible to the vein insertion.

Moderate anxiety disorders and symptoms of anxiety, 2 to 5 mg I.M. or I.V., and severe anxiety disorders and symptoms of anxiety, 5 to 10 mg I.M. or I.V., repeat in 3 to 4 hours if necessary; acute alcohol withdrawal, 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary. Muscle spasm, in adults, 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary (tetanus may require larger doses); in children administer I.V. slowly; for tetanus in infants over 30 days of age, 1 to 2 mg I.M. or I.V., repeat every 3 to 4 hours if necessary; in children 5 years or older, 5 to 10 mg repeated every 3 to 4 hours as needed. Respiratory assistance should be available.

Status epilepticus, severe recurrent convulsive seizures (IV route preferred), 5 to 10 mg adult dose administered slowly; repeat at 10- to 15-minute intervals up to 30 mg maximum. Repeat in 2 to 4 hours if necessary; keeping in mind possibility of residual active metabolites. Use caution in presence of chronic lung disease or unstable cardiovascular status. Infants (over 30 days) and children (under 5 years), 0.2 to 0.5 mg slowly every 2 to 5 min., up to 5 mg (IV preferred). Children 5 years plus, 1 mg every 2 to 5 min., up to 10 mg (slow IV preferred); repeat in 2 to 4 hours if needed. EEG monitoring may be helpful.

In endoscopic procedures, titrate IV dosage to desired sedative response, generally 10 mg or less but up to 20 mg (if narcotics are omitted) immediately prior to procedure; if I.V. cannot be used, 5 to 10 mg I.M. approximately 30 minutes prior to procedure. As preoperative medication, 10 mg I.M.; in cardioversion, 5 to 15 mg I.V. within 5 to 10 minutes prior to procedure. Once acute symptomatology has been properly controlled with injectable form, patient may be placed on oral form if further treatment is required.

**Management of Overdosage:** Manifestations include somnolence, confusion, coma, diminished reflexes. Monitor respiration, pulse, blood pressure; employ general supportive measures, IV fluids, adequate airway. Use levaterenol or metaraminol for hypotension. Dialysis is of limited value.

**How Supplied:**

**ORAL:** Valium scored tablets—2 mg, white; 5 mg, yellow; 10 mg, blue—bottles of 100 and 500; Prescription Paks of 50, available in trays of 10; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25 and in boxes containing 10 strips of 10.

Valrelease (diazepam/Roche) slow-release capsules—15 mg (yellow and blue), bottles of 100; Prescription Paks of 30.

**INJECTABLE:** Ampuls, 2 ml, boxes of 10; Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.





# Acute Upper Gastrointestinal Bleeding in Children

Eduardo Cichowicz, M.D.  
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**Summary** This review is an attempt to bring to the pediatrician's attention up-to-date concepts regarding the diagnosis and management of acute upper gastrointestinal bleeding in children. The value of endoscopy as a first-line diagnostic procedure is underscored along with the limitations of more traditional tests. The common causes of hematemesis in pediatrics are discussed briefly, with emphasis on current concepts of peptic ulcer disease as they relate to children, including the role, if any, of aspirin, steroids and stress. Finally, different aspects of initial management of these children are discussed, with emphasis on gastric lavage, the use of antacids, and how to deal with patients who continue to bleed after conservative management.

This review is primarily intended to bring pediatricians and other physicians who work with children up to date on a topic which is rarely discussed from a pediatric perspective. As most of the significant progress related to gastrointestinal bleeding and endoscopy appears in the non-pediatric literature, pediatricians may still be unaware of material which by now is old-hat to the internist.

An effort has been made to remain as practical as possible and to establish guidelines for management when the literature permits. Long-held concepts of diagnosis and management regarding the patient with upper gastrointestinal bleeding (UGIB) have of recent been largely abandoned or seriously questioned, and these will be brought to the attention of the reader. The information will be divided into three sections. We will begin with a presentation of the diagnostic modalities available to localize bleeding sites, followed by a summary of the most common causes of hematemesis in children, and finish with a discussion of the early management of these patients.

## Diagnostic Modalities

As residents who enjoy the services of a pediatric gastroenterologist soon discover, the history of present illness and physical exam are usually of little help in correctly anticipating the upper intestinal lesion from which an infant

or child has just bled. The caveats from internal medicine regarding typical histories in patients with ulcer disease, gastritis, Mallory-Weiss tears and the like, are seen to be inapplicable to children and soon discarded. The routine upper gastrointestinal series (UGIS) is likewise noted not to correlate sufficiently well with endoscopy, and is slowly but surely relegated to an ancillary role, to be used in the few children where endoscopy has not produced a diagnosis.

Internists have for years been proving that, in cases of UGIB, there is just no substitute for actually observing the lesion fiberoptically. The routine use of upper endoscopy in children was held up by the need to establish that the procedure was safe and reliable in the pediatric age group. This having been shown,<sup>1-8</sup> endoscopy is now the accepted first-line procedure for all cases of acute UGIB in children, from neonates to adolescents. It's routine use is now redefining the pathology associated with UGIB in pediatrics.

Table 1 lists how positive diagnoses were made in children with UGIB when comparing barium studies and endoscopy. It is evident from these numbers that endoscopy is by far the more reliable diagnostic test, with some authors reporting diagnostic accuracy close to 100%.

TABLE I

### Diagnoses Established by Barium Studies (UGIS) and Endoscopy in Children with UGIB

Authors	UGIS	Endoscopy
Gleason et al, 1974 <sup>6</sup>	0/10	10/10
Tedesco et al, 1976 <sup>4</sup>	10/24	20/24
Liebman, 1977 <sup>7</sup>	12/18	17/18
Ament et al, 1977 <sup>3</sup>	6/43	35/43
Graham et al, 1978 <sup>8</sup>	4/20	13/20
Cox et al, 1979 <sup>1</sup>	21/47	28/33
Totals	53/162	123/148

An UGIS is not reliable in children who have bled from the upper gastrointestinal (GI) tract for a number of important reasons. First of all, there simply is a spectrum of significant pathology that cannot be adequately observed. Esophagitis, erosive gastritis and Mallory-Weiss tears, for example, are in this category.<sup>9</sup> This is a clear handicap in a population where easily picked up mass lesions are distinctly rare and most bleeding sites are superficial erosions (easily seen at endoscopy).

Second, and more important, signs of recent hemorrhage can only be picked up by special techniques (double contrast).<sup>10</sup> It should be very clear to the physician-in-charge that identifying an abnormality during a routine UGIS in no way guarantees that it is, in fact, the source of blood loss.<sup>9</sup> For example, only 50% of children who have varices, and UGIB, are actually acutely bleeding from the varices.<sup>2</sup> An UGIS which in these circumstances confirms varices is just not good enough in terms of planning short and long term management. Absolute proof that varices have bled is essential, for instance, in the decision to perform an elective therapeutic

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portosystemic shunt. If variceal hemorrhage has not been documented, a shunt is classified as prophylactic, and these are not recommended.<sup>11</sup> Endoscopy becomes mandatory, then in these children.

The importance of this second deficiency with respect to roentgenographic diagnosis was exemplified by Keller et al,<sup>12</sup> whom randomized the sequence of endoscopy and UGIS, performed within two days of admission, and analyzed the effect of the respective diagnosis on patient management. Endoscopy had a uniformly favorable effect, whereas x-ray findings had a detrimental one on clinical management. In other words, correct management was changed to incorrect management by x-ray results more frequently than errors in management were corrected.

The angiographic diagnosis of UGIB depends on visualization of extravasation of the contrast agent into the gastrointestinal lumen. Angiography does present certain advantages over endoscopy.<sup>13</sup> It does not require a great deal of patient cooperation, it can be performed on very ill patients, it does not require special preparation, accurate diagnosis can be made despite the presence of active bleeding and of large amounts of blood in the GI tract, and lastly, it allows for transcatheter therapy. Successful visualization, however, requires a child bleeding at a minimum rate of 0.5 ml per minute at the time of contrast material injection.<sup>14</sup>

When considering angiography, it is important that reasonable expectations be had regarding its usefulness. Angiography can most easily demonstrate arterial bleeding, as from a peptic ulcer. Super selective angiograms can show minor (capillary) sources of hemorrhage, as could be present in erosive gastritis or stress ulcers.<sup>15</sup> Venous bleeding, however, is almost never demonstrated by arteriography even when patients are examined during massive bleeding from esophageal varices.<sup>13</sup> In addition, because of the intermittent nature of GI bleeding, arteriography will not be diagnostic if the study is performed between bleeding episodes. Lastly, if angiographic techniques are to be effective in the management of sudden UGIB, the studies should be performed efficiently and rapidly by personnel who must be available 24 hours a day and on short notice. As Baum<sup>13</sup> points out, this represents a major commitment of resources on the part of a radiology department.

To conclude this segment, our recommendations for the diagnostic workup of a child with UGIB are as follows. There is a general consensus that endoscopy should be the first diagnostic procedure attempted, or at least considered, in all cases, at all ages. The best chance of finding the bleeding lesion is by performing endoscopy within 12 hours of the initiation of the bleeding episode,<sup>9</sup> although a high level of diagnostic accuracy seems to be retained for at least 48 hours.<sup>16</sup> Endoscopy may be decided against in two clinical situations. First, one may be relatively secure in assuming that certain critically ill children (burned, uremic, head-trauma) will be bleeding from gastric erosions or gastric or duodenal ulcers. Endoscopy in these children will not affect medical therapy and is indicated only if bleeding does not decrease within several hours or totally respond within 24 hours.<sup>2</sup> The other situation involves the child with continuous bleeding, in whom it is anticipated that blood will likely obscure the endoscope's field of view and in whom aspiration of blood is a possibility. The major contribution of angiography, is in the diagnosis and management of patients in whom the bleeding does not stop after conservative

methods are used, and in whom surgical intervention is contemplated.<sup>13</sup> Where facilities exist for both endoscopy and emergency angiography, there is little place for barium studies in the management of UGIB, since the presence of barium in the abdomen precludes the use of angiography for several days.<sup>17</sup> If angiography is not feasible or indicated, then double contrast barium studies may be undertaken in the roughly 10% of patients where endoscopy has not found a lesion. Isotopic scanning is generally of limited value in locating bleeding sites above the ligament of Treitz. The two radionuclide studies most commonly used in this respect will be discussed in a subsequent review on lower GI bleeding in children.

### Causes of UGIB in Children

Table II lists the more common causes of UGIB in children along with some possible pathogen mechanisms involved. The conditions are not listed in order of frequency, since the most common causes will be seen to vary with age (Table III). The individual conditions will now be treated separately in some measure. For purposes of discussion, however, "stress-related" bleeding will be handled separately. Since the discussion of each cause will not be extensive, the interested reader is referred to the appropriate references for more detail.

TABLE II

Common Causes of UGIB in Children (not in order of frequency)	
1. Esophageal Varices	—portal vein thrombosis
2. Esophagitis	—gastroesophageal reflux —infectious
3. Gastritis/Duodenitis	—drugs —metabolic-injury stress
4. Peptic Ulcer Disease	—primary —metabolic-injury stress
5. Foreign Body Ulceration	
6. False UGIB (swallowed blood)	

1. *Esophageal varices*: Portal hypertension should be considered the most probable diagnosis in any child with hematemesis in whom the spleen is palpable. In the adult, portal hypertension is usually the outcome of intrahepatic obstruction due to cirrhosis, but in the child, extrahepatic obstruction due to portal vein thrombosis is the more common cause. If, in addition, the liver is enlarged, congenital hepatic fibrosis should be considered.<sup>18 19</sup> Esophageal vari-



ces have been seen to be present, but not to be bleeding, in fiberoptic examinations of infants under one year of age.<sup>2</sup>

2. *Esophagitis*: Different reports on causes of UGIB in pediatrics have found esophagitis to be an important lesion at all ages. Unfortunately, there is little information regarding etiologic factors involved in producing esophagitis in the setting of UGIB. What percent of children who bleed from esophagitis have underlying lower esophageal sphincter dysfunction versus an infectious esophagitis has not been adequately reported.

With the routine use of the standard acid reflux test (Tuttle test) and prolonged (24 hour) esophageal pH monitoring, pediatricians have become aware of the high incidence of gastroesophageal reflux in infants and its associated morbidity.<sup>20</sup> Accordingly, reflux-induced esophagitis is receiving considerable attention in the literature recently.<sup>21-23</sup> Just how often reflux-induced esophagitis progresses to hematemesis in infants, though, is just not clear. Although a recent review of the literature for children at all ages revealed that bleeding from the GI tract occurred in 28% of children with gastroesophageal reflux,<sup>24</sup> it is not noted how many of these presented with anemia and melena and not hematemesis. Leape et al<sup>25</sup> have presented evidence to suggest that infants with documented gastroesophageal reflux rarely have severe esophagitis. Prospective studies of children with gastroesophageal reflux are needed to see how many, in fact, progress to UGIB.

3. *Gastritis/Duodenitis*:<sup>26</sup> Gastroduodenitis may be the most common cause of UGIB in infants,<sup>7</sup> and is certainly an important cause throughout the rest of childhood. In spite of this, the factors responsible for a gastroduodenal inflammation severe enough to cause hematemesis in a child are not well established. There is, nevertheless, a strong clinical impression that certain commonly used oral medications are directly responsible for bleeding gastroduodenitis in some children. Aspirin, aminophylline and steroids are the most frequently mentioned. Here we will review the case for aspirin and aminophylline. Steroids will be discussed under the peptic ulcer disease heading.

Although there is little question that aspirin does cause both micro and macroscopic erosions of the gastroduodenal mucosa in some children<sup>27,28</sup>, there is debate as to the importance of aspirin as a causative factor in a population of children with UGIB. Some authors are so convinced of the probable cause-effect relationship that they do not recommend endoscopy in children with hematemesis when there is a history of recent aspirin intake.<sup>2</sup> We have personally seen too many cases of unsuspected lesions, including varices, esophagitis, hemangiomas and even tumors, to support this point of view. Almost all children who complain of feeling very ill receive aspirin products sooner or later. We agree with Turnberg and Rees,<sup>29</sup> that, faced with a patient with acute hematemesis and a history of aspirin intake, it would be unwise to assume aspirin is the cause of the bleeding. There is evidence to suggest that in only one of three patients who have bled and recently taken aspirin, will the cause of hemorrhage be determined to be aspirin.<sup>30</sup> Our practice is therefore to recommend endoscopy in all children with significant UGIB, regardless of the aspirin intake history.

Products containing aminophylline have long been known to cause stomach upset and "gastritis", but there is surprisingly little information directly correlating them with UGIB.

Foster et al<sup>31</sup> have confirmed that aminophylline causes a significant increase in basal acid output from the stomach, probably mediated through increased gastrin levels. The two patients reported by Mackay et al,<sup>32</sup> who had UGIB while being treated with continuous-release aminophylline tablets, had, interestingly enough, not gastritis, but acute ulcerations of the duodenum and lower esophagus, respectively. Most pediatricians have had experience with children who, a couple days after first initiating oral aminophylline, complain of stomach ache and may eventually vomit up some coffee-ground material. These patients can probably be safely managed by discontinuing aminophylline in favor of another bronchodilator and giving a short course of antacids. However, any child who has been taking aminophylline regularly or irregularly in the past and who presents with UGIB, unquestionably needs endoscopy. The literature is too vague at this time to know what percentage of aminophylline using children are prone to UGIB.

Apart from drug-induced gastritis, hematemesis in children is all too often attributed to "viral gastritis". There is, in fact, no evidence to substantiate that viral infections of the gastric mucosa commonly take place, akin to rotavirus or Norwalk agent<sup>33</sup> invasion of the small intestine. That viruses cause bleeding gastric lesions, then, is conjecture at this point in time, and the designation "viral gastritis" should be abandoned in pediatrics. Remember that gastritis is an impression received at endoscopy and confirmed only at biopsy. Attributing an episode of UGIB to gastritis on clinical grounds is shaky at best, specially in children. Even in adults, studies have confirmed that one cannot clinically differentiate gastroduodenitis from peptic ulcer disease.<sup>34</sup>

4. *Peptic Ulcer Disease (PUD)*: Once thought to be extremely rare in pediatrics, PUD is now known to occur in infancy, including the neonatal period, and there is some evidence<sup>1</sup> that, after the first year of life, PUD is the most common cause of UGIB in children. Various studies<sup>35,36</sup> seem to indicate that 80% of ulcers in infancy can be attributed directly to an underlying pathology or metabolic stress. After infancy, however, 70% of ulcers in children appear to be spontaneous, or primary. There is conflicting data as to whether ulcers in children are more frequently gastric or duodenal.<sup>36,37,38</sup> It is probably safe to say that primary ulcers are more commonly gastric in the preschool years and duodenal afterwards.

It is now believed that childhood duodenal ulcer may be distinct genetically from adult duodenal ulcer, analogous to the separation of juvenile-onset from maturity-onset diabetes.<sup>39</sup> Investigators have been impressed by the frequency of a "positive family history", with first and second degree relatives of childhood duodenal ulcer patients affected twice as frequently as relatives of adult probands.<sup>40</sup> Additionally, children with duodenal ulcer have a frequency of blood group 0 similar to that of controls, an increased frequency of UGIB as the first manifestation of the disease (88%), and a paucity of other complications such as perforation, obstruction, intractable pain or secondary gastric ulcer.<sup>41</sup>

Zollinger-Ellison syndrome (gastrinoma) is known to occur in children.<sup>42</sup> Regan and Malagelada<sup>43</sup> have recently pointed out that the clinical manifestations of Zollinger-Ellison syndrome seen today are often inconspicuous, presenting as uncomplicated duodenal ulcer or even as erosive duodenitis with minimal roentgenographic abnormalities. In fact, none of their patients had ulcers in atypical locations

(esophagus, distal duodenum or jejunum). In view of these findings, we concur with Nord and Lebenthal<sup>44</sup> that all children with peptic ulcer disease deserve a fasting serum gastrin determination.

Finally, PUD is mentioned frequently in pediatrics with respect to children suffering from juvenile rheumatoid arthritis (JRA) and taking steroids. The literature in this respect has been reviewed many times and different authors have drawn widely different conclusions from the same body of evidence.<sup>45</sup> Reviewing a number of prospective and retrospective studies, Cooke<sup>46</sup> concludes that patients with rheumatoid arthritis possibly have a higher frequency of PUD, the cause of which is unclear. While some authors<sup>47</sup> have reported an incidence of nearly 30% in adults, Brewer et al's recent book<sup>48</sup> on JRA proclaims that PUD in these children is seen only rarely.

The case for steroids has at times been just as confusing, but recent studies<sup>49, 50</sup> have demonstrated that corticosteroids do not, in fact, increase the prevalence of peptic ulceration. Neither has there been an increased incidence of hemorrhage and/or perforation of existing ulcers while on steroids. There is general agreement, however, that steroids allow a perforation to be "silent", but this impression has not been critically evaluated.<sup>46</sup> The available evidence, then, encourages the use of diagnostic endoscopy in children with UGIB who have JRA or are taking steroids, or both. Assuming PUD in these cases cannot be supported by the literature at this time.

5. *Stress and UGIB:* We have chosen to discuss the effects of stress on the upper GI tract separately, since the proposed lesions encompass gastric erosions to duodenal ulcers. A distinction will be made between life-stress and what we have chosen to call metabolic injury stress. The association of life-stress and PUD has received considerable attention in the adult literature, but has not been investigated consistently in pediatrics. There is some evidence that certain personality characteristics may be more prevalent in children with PUD, but the studies are far from conclusive.<sup>44</sup> Likewise, it has been thought that PUD frequently occurs in those individuals subjected to excessive pressure in their daily lives, but there is no convincing evidence that this is true, in adults or in children.<sup>51, 52</sup>

Certain physiologically stressful injuries or disease states, on the other hand, are well known to cause upper GI lesions, even though the mechanisms that lead to these focal destructions of epithelium are still speculative. This is a most important problem, since in both adults and infants, when there is massive bleeding from a stress-induced lesion, the mortality is from 30-40%.

In the adult, and presumably in older children, the products of metabolic-injury stress are usually multiple superficial gastric erosions in the fundus which rarely perforate. In contrast, young infants subjected to similar stress appear to have a higher incidence of single ulcers in the duodenum, and these are prone to perforate.<sup>53</sup> Although upper GI lesions may be common in infants and children with metabolic-injury stress, evidence of UGIB is frequently lacking. Johnson et al<sup>54</sup> report 12 young infants who had evidence of perinatal and/or neonatal stress and who developed PUD. Only four of these infants presented with hematemesis, the other eight having only chronic regurgitation. Bell et al<sup>55</sup> reports ten infants less than one year of age with gastroduodenal perforation during treatment for severe underlying illnesses. Hematemesis preceded the perforation in only three, and melanic or bloody stools were present in three others. Pediatricians, then, cannot afford to wait for proof of UGIB before considering the

possibility of stress-induced PUD and perforation, especially in infants.

Acute mucosal changes are common in patients who have suffered massive burns and other major physical trauma (up to 90% of patients in some series<sup>55, 56</sup>) but such lesions rarely bleed.<sup>59</sup> Other conditions seen in pediatrics which are associated with stress lesions of the GI tract and UGIB are uremia and malignancies. Mucosal abnormalities of the gut are present in up to 60% of patients with uremia, with multiple acute ulcers of the stomach and duodenum being relatively common.<sup>57</sup> Hemorrhagic gastritis is the most frequent cause of UGIB in patients with cancer. Patients with hematologic malignancy appear to be particularly prone to stress ulcer bleeding. Chemotherapeutic agents such as 5-fluorouracil, cyclophosphamide, methotrexate and bleomycin have significant gastrointestinal side effects, but have been infrequently associated with gastroduodenal ulceration.<sup>58</sup>

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TABLE III

Most Common Causes of UGIB by Age	
Infancy:	Gastritis Esophagitis
2-6 years:	Gastric Ulcer Esophagitis
School age:	Duodenal Ulcer Gastritis

To summarize this section, then, life-stress and metabolic-injury stress should be considered differently in terms of probable association with UGIB. One cannot confidently attribute a bleeding ulcer in a child to his personality or his environmental demands. Certain disease states and injuries do frequently induce upper GI pathology, predominantly fundal erosions, but UGIB, the hallmark of stress-associated lesions, is probably uncommon in children. Young infants may bleed more often, but other signs, such as recurrent emesis, present at least as frequently. The need for endoscopy in children with metabolic injury stress and UGIB is not absolute and should be seriously considered only if bleeding cannot be controlled in a reasonable time. Even then, angiography may be the procedure of choice depending on the child's condition.

### Acute Management of UGIB

Any pediatric age patient who presents with evidence of UGIB deserves prompt hospitalization and pediatric gastroenterologic consultation to assess the need for endoscopy. The first line of management is clear: good venous access, monitoring of vital signs, serial hematocrits, determination of coagulation parameters and possibly cross-matching blood. Additional maneuvers should always include dropping a large-bore nasogastric tube and removing residual blood. The stomach should then be washed briefly with room temperature saline and subsequently decompressed, with the nasogastric tube being removed if active bleeding has stopped.

Iced saline gastric lavage is a time-honored but doubtful procedure which may, in fact, be detrimental. A number of



investigators have shown that the application of low temperature to bleeding wounds will prolong the bleeding time.<sup>60 61</sup> Ponsky et al<sup>62</sup> have recently shown that iced saline irrigation in gastric hemorrhage is significantly less effective in promoting hemostasis than irrigation with room temperature saline. Even more surprising, removal of shed blood without irrigation provided cessation of hemorrhage more rapidly than with irrigation at any temperature. Limited irrigation, however, should be carried out, as it helps document termination of active bleeding and rids the gastric mucosa of blood which will interfere with endoscopic interpretation. Vigorous and prolonged lavage may disrupt fibrin clots and is to be discouraged.

Nasogastric tubes should not be routinely left in place, since within a few hours, artifacts may be produced in the gastric mucosa which may be difficult to distinguish endoscopically from true erosive lesions. This practice, of course, must be tempered in children by the need to give repeated antacid doses in a non-cooperative patient. Later, if one suspects that a significant amount of blood has reaccumulated, the stomach should be washed and decompressed again prior to endoscopy to prevent possible aspiration of blood during intubation and permit good visualization thereafter. There is no contraindication to passing a nasogastric tube in a child with UGIB in whom esophageal varices are a possibility.

Virtually all cases of UGIB in children can be treated by removal or neutralization of gastric acid. For this purpose, antacids and cimetidine have been the most used drugs. The case for antacids seems well founded, but cimetidine probably does not have a role in treating or preventing UGIB.

Hastings et al<sup>63</sup> reported a controlled randomized trial in 100 critically ill patients at risk of developing acute GI ulceration and bleeding. One group received antacid prophylaxis (hourly titration kept pH of gastric contents above 3.5) and the other group no specific form of prophylaxis. Two of 51 patients receiving antacids and 12 of 49 controls bled ( $p < 0.005$ ). It was concluded that the occurrence of acute GI bleeding in critically ill patients can be reduced by antacid titration. Priebe et al<sup>64</sup> report a randomized trial in 75 critically ill patients where one group received cimetidine intravenously at 300 mg every six hours and another group received an antacid (Mylanta II) via a nasogastric tube at an initial dose of 30 ml every hour. Gastric pH was measured hourly and titrated above 3.5 UGIB occurred in seven of 38 cimetidine-treated patients and in none of 37 antacid-treated patients ( $p < 0.01$ ). The conclusion was that cimetidine does not adequately protect seriously ill patients from acute UGIB. Antacids were better for this purpose.

Backing up these conclusion is a report from Stothert et al<sup>65</sup> who studied 144 critically ill patients in a randomized prospective fashion. Cimetidine was given at an initial dose of 300 mg every six hours to one group of adults and the dosage was increased up to 2400 mg/24 hours if the pH of gastric contents was consistently under 4.0. The other group received sufficient hourly Mylanta II to keep the gastric pH above 4.0. In all 58 patients receiving antacids alone, an average of 41ml/hour maintained the pH at 4.0, while only 47% of these receiving the routine and 74% of those in the maximal cimetidine dose attained consistent protection against gastric acidity.

Although these studies involve preventing stress ulcerations in critically ill adults, we believe that the management goals desired in children with UGIB remain the same, reduce the

acid content of the stomach to prevent ongoing ulceration. In this regard, then, cimetidine does not appear to be a drug of choice and vigorous treatment with antacids does seem to be justified.

We recommend a product similar to Mylanta II in acid neutralizing capacity, at an initial dose of 30 ml per hour for children older than 5 years, and 10-20 ml per hour for infants and younger children. The hourly dosage should probably be continued for 48 hours after the bleeding has subsided and then given one and three hours after meals throughout the remainder of their hospitalization.<sup>1</sup> A given dose may be doubled every hour during the initial period until gastric aspirates show a pH of at least 3.5.

The great majority of UGIB episodes in children, even hemorrhages from esophageal varices, stop spontaneously and require only supportive therapy. For the occasional child who continues to bleed, the pediatric literature has not established a uniform management protocol. This is most likely due to the fact that each center will manage a bleeding child depending on the expertise it has available in one of two or three modalities.

If there is a radiologist competent in pediatric angiography at your disposition, diagnostic and therapeutic arteriography may be attempted. Should this procedure be impossible to arrange, a short trial of vasopressin via-continuous peripheral intravenous infusion sometimes is successful. There is some evidence<sup>66 67</sup> to suggest that intravenous vasopressin may be as effective as intra-arterial infusions for variceal bleeding and some workers<sup>68 69</sup> believe vasoconstrictor therapy may be effective in non-variceal bleeding as well. The pediatrician should realize, however, that vasopressin may lull the attending physician into postponing needed surgery. A decreased pulse rate is often taken as a sign of circulatory stabilization, but bradycardia is a recognized effect of systemic vasopressin<sup>70</sup> and can mimic improvement. In addition, recurrent hemorrhage has been reported in 45-70% of adult patients who initially stopped bleeding with vasopressin. Finally, complications of systemic vasoconstrictor therapy can be serious and its administration should be closely supervised, in an intensive care unit if possible.

Should esophageal varices be endoscopically or angiographically confirmed to be the site of continued blood loss, a physician with experience in using balloon tamponade in children may be called on. While use of a Sengstaken-Blakemore tube is fraught with significant complications such as lacerations, necrosis, aspiration and perforation, some centers<sup>71</sup> report it to be the method of choice for early control of variceal hemorrhage.

Surgery should be undertaken in children with UGIB if more than 85 ml per kg of blood have been transfused within 90 minutes.<sup>1</sup> Experience during the last decade indicates that only 2% of infants with UGIB require surgical intervention.<sup>2</sup> We have found no comparable numbers for children and adolescents. When patients do come to surgery following a negative endoscopic examination, they are usually found to be bleeding from a tiny erosion high in the body of the stomach or from lesions distal to the ligament of Treitz.<sup>9</sup> Lastly, the following factors have been associated with increased mortality in children with UGIB: the co-existence of another severe medical disorder, failure to identify the bleeding site, a hemoglobin of less than 7gm and more than 85ml per kg of blood loss without surgical intervention.<sup>1</sup>

## Conclusions

Fiberoptic endoscopy is today the accepted procedure-of-choice for use in diagnosing the source of UGIB in children of all ages. A routine UGIS cannot detect signs of recent hemorrhage and is therefore unreliable for this purpose. The major use of angiography is in patients in whom bleeding does not stop after conservative management, and in whom surgical intervention is contemplated. The most common cause of UGIB in infancy is erosive gastroduodenitis, while in older children gastric and duodenal ulcer disease predominate. There is a strong clinical impression that some erosive bleeding lesions in children are due to aspirin and aminophylline-containing medications, but how much these drugs contribute to a population of children with UGIB is controversial. Childhood duodenal ulcer disease appears to be distinct genetically from adult duodenal ulcer disease. Juvenile rheumatoid arthritis and steroids have in the past been thought to predispose to PUD, but these contentions are now doubted seriously. There is no convincing evidence that personality or life-stress predisposes children to PUD. However, certain injuries and/or disease states do appear to regularly cause fundal erosions, but these uncommonly manifest as frank UGIB. Disease-related stress in young infants, though, seems to produce a higher incidence of solitary duodenal ulcers prone to perforate, and often not associated with UGIB.

Any pediatric age patient who presents with UGIB deserves prompt hospitalization and endoscopic evaluation of the site of hemorrhage should be planned for the initial 48 hours. If the cause of bleeding is a mucosal erosion, associated or not with PUD, or if the site of bleeding is unknown, these children are best treated with hourly antacids. Cimetidine has not proven advantageous in preventing UGIB. The management of a child who continues to bleed depends to a great extent on the procedural expertise of available specialists. Surgery should be undertaken if more than 85ml per kg of blood are transfused within 90 minutes.

**Resumen:** Este repaso intenta traer a la atención del pediatra conceptos recientes en lo que concierne el diagnóstico y manejo de niños con sangramiento intestinal alto. La importancia de la endoscopia como procedimiento diagnóstico primario se subraya y al igual, se mencionan las limitaciones de pruebas tradicionales en este respecto. Se discuten brevemente las causas mas comunes de hematemesis en las edades pediátricas, con énfasis en nuevos conceptos de enfermedad de úlcera péptica en niños y el rol, si alguno, de la aspirina, los esteroides y el stress. Finalmente, se discuten aspectos diferentes del manejo inicial de estos niños, especialmente en lo concerniente a el lavado gástrico, el uso de antiácidos y el paciente con hemorragia persistente.

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## ASOCIACION PUERTORRIQUEÑA DEL CORAZON

MAS DE \$37,000 PARA INVESTIGACION

FECHA LIMITE PARA SOLICITAR: 1 de octubre de 1983.

REQUISITOS: Grados de doctor (M.D.; Ph.D: D.D.S.; D.V.M. o su equivalente).

Asistencia económica hasta \$15,000 al año por persona para investigación en el campo cardiovascular, incluyendo investigación clínica, epidemiología y problemas relacionados con las ciencias básicas.

INFORMESE CON:

Mildred Alejandro Merced  
Directora de Programa  
Asociación Puertorriqueña del Corazón  
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## BRIEF SUMMARY

### PROCARDIA® (nifedipine) CAPSULES

For Oral Use

**INDICATIONS AND USAGE:** I. **Vasospastic Angina:** PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. **Chronic Stable Angina (Classical Effort-Associated Angina):** PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in those patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

### **CONTRAINDICATIONS:** Known hypersensitivity reaction to PROCARDIA

**WARNINGS: Excessive Hypotension:** Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out. In PROCARDIA treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for PROCARDIA to be washed out of the body prior to surgery.

**Increased Angina:** Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PROCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

**Beta Blocker Withdrawal:** Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

**Congestive Heart Failure:** Rarely, patients usually receiving a beta blocker, have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

**PRECAUTIONS: General: Hypotension:** Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See Warnings.)

**Peripheral edema:** Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

**Drug interactions:** Beta-adrenergic blocking agents. (See Indications and Warnings.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates. PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis. Administration of PROCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PROCARDIA to avoid possible over- or under-digitalization.

Carcinogenesis, mutagenesis, impairment of fertility. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose.

Pregnancy. Category C. Please see full prescribing information with reference to teratogenicity in rats, embryotoxicity in rats, mice and rabbits, and abnormalities in monkeys.

**ADVERSE REACTIONS:** The most common adverse events include dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients; transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antianginal medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, diarrhea, constipation, inflammation, joint stiffness, shakiness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, and sexual difficulties. Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

**Laboratory Tests:** Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CPK, LOH, SGOT, and SGPT have been noted, and a single incident of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PROCARDIA therapy is uncertain. These laboratory abnormalities have rarely been associated with clinical symptoms. Cholestasis, possibly due to PROCARDIA therapy, has been reported twice in the extensive world literature.

**HOW SUPPLIED:** Each orange, soft gelatin PROCARDIA CAPSULE contains 10 mg of nifedipine. PROCARDIA CAPSULES are supplied in bottles of 100 (NDC 0069-2600-66), 300 (NDC 0069-2600-72), and unit dose (10x10) (NDC 0069-2600-41). The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

More detailed professional information available on request.

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# *"I can do things that I couldn't do for 3 yrs. including joining the human race again."*



*Quotes from an unsolicited  
letter received by Pfizer from an  
angina patient  
While this patient's experience  
is representative of many  
unsolicited comments received,  
not all patients will respond to  
Procordia nor will they all  
respond to the same degree.*

*"My daily routine consisted of  
sitting in my chair trying to stay alive."*

*"My doctor switched me to  
PROCARDIA[\*] as soon as it became  
available. The change in my condition  
is remarkable."*

*"I shop, cook and can plant  
flowers again."*

*"I have been able to do volunteer  
work...and feel needed and useful  
once again."*

PROCARDIA can mean the return to a more normal life  
for your patients—having fewer anginal attacks,<sup>1</sup> taking  
fewer nitroglycerin tablets,<sup>2</sup> doing more, and being more  
productive once again.

Side effects are usually mild (most frequently reported  
are dizziness or lightheadedness, peripheral edema,  
nausea, weakness, headache and flushing, each occurring  
in about 10% of patients, transient hypotension in about  
5%, palpitation in about 2% and syncope in about 0.5%).



*for the varied faces of angina*

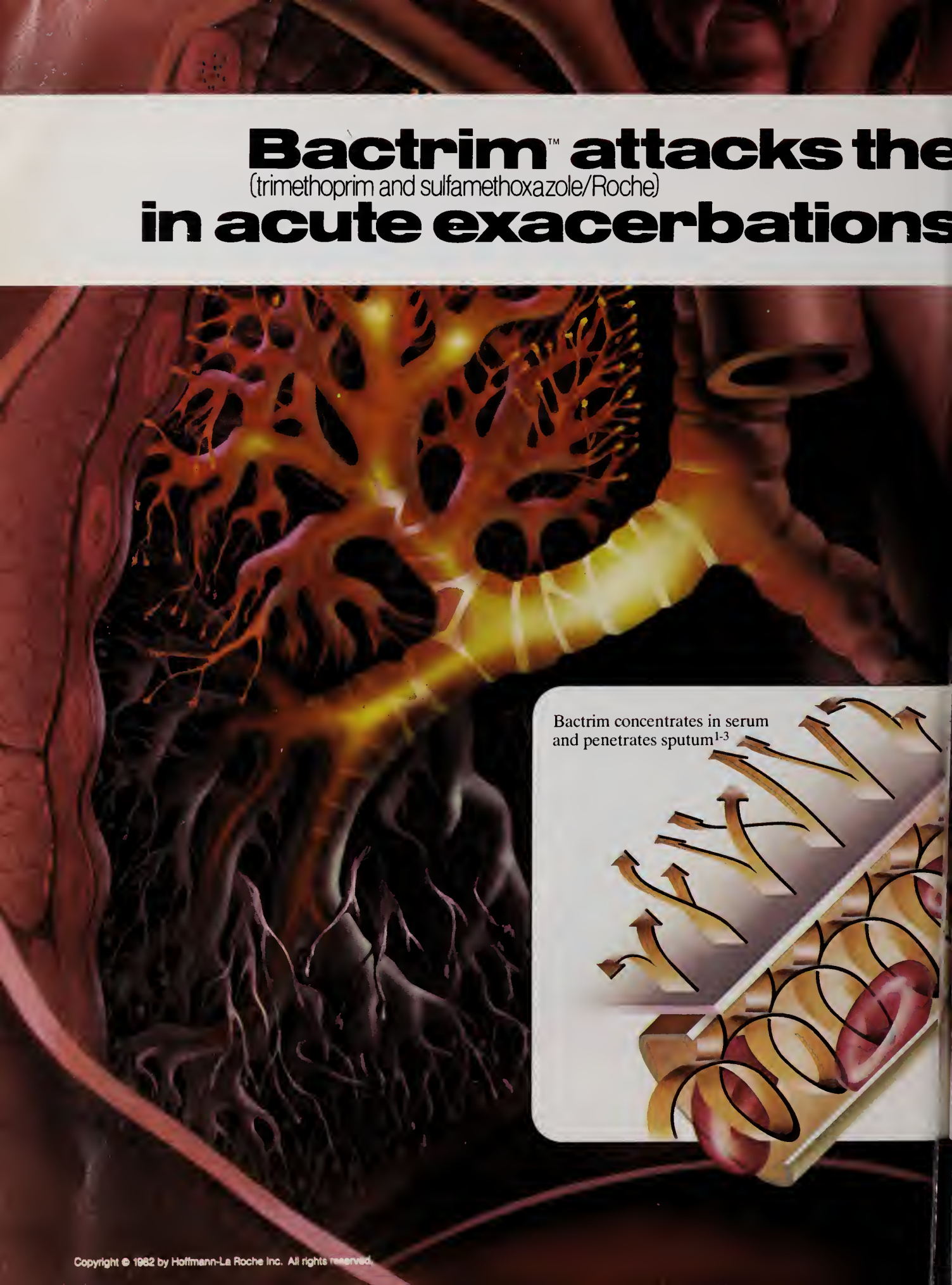
## **PROCARDIA<sup>®</sup>** **(NIFEDIPINE)** Capsules 10 mg

\*Procordia is indicated for the management of:

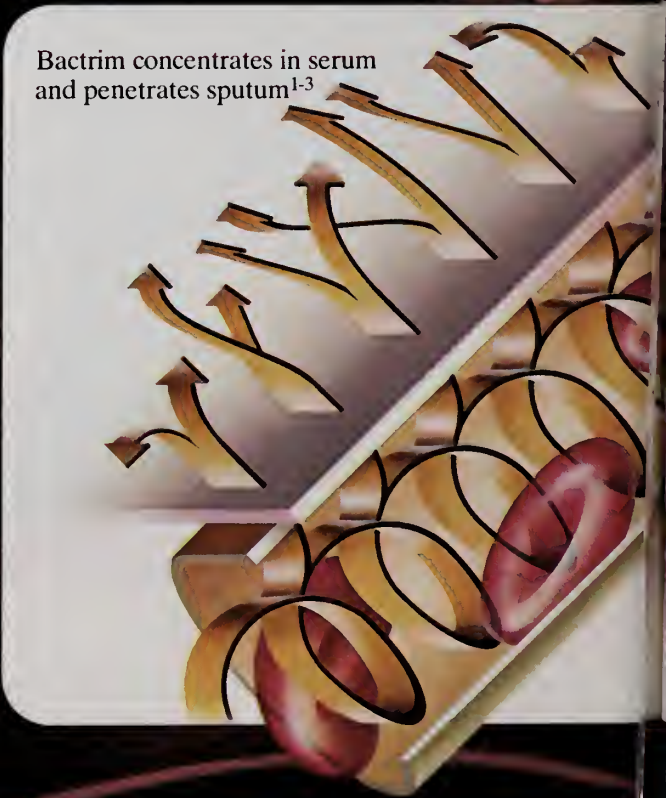
- 1) Confirmed vasospastic angina.
- 2) Angina where the clinical presentation suggests a possible vasospastic component.
- 3) Chronic stable angina without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or nitrates or who cannot tolerate these agents. In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks' duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete.

*Please see PROCARDIA brief summary on adjoining page*

# **Bactrim™ attacks the** (trimethoprim and sulfamethoxazole/Roche) **in acute exacerbations**



Bactrim concentrates in serum  
and penetrates sputum<sup>1-3</sup>





# major pathogens of chronic bronchitis\*

## Bactrim clears sputum of susceptible bacteria

In sputum cultures from patients with acute exacerbations of chronic bronchitis, *H. influenzae* and *S. pneumoniae* are isolated more often than any other pathogens.<sup>4,5</sup> One study of transtracheal aspirates from 76 patients with acute exacerbations found that 80% of the isolates were of these two pathogens.<sup>5</sup>

Bactrim is effective *in vitro* against most strains of both *S. pneumoniae* and *H. influenzae*—even ampicillin-resistant strains. And in acute exacerbations of chronic bronchitis involving these two pathogens, sputum cultures taken seven days after a two-week course of therapy showed that Bactrim eradicated these bacteria in 91% (50 of 55) of the patients treated.<sup>6</sup>

## Bactrim reduces coughing and sputum production

In three double-blind comparisons with ampicillin *q.i.d.*, Bactrim DS proved equally effective on all clinical parameters.<sup>7-9</sup> Bactrim reduced the frequency and severity of coughing, reduced the amount of sputum produced and cleared the sputum of purulence.

Bactrim has the added advantages of *b.i.d.* dosage convenience and a lower incidence of diarrhea than with ampicillin, and it is useful in patients allergic to penicillins.

Bactrim also proved more effective than tetracyclines in 10 clinical trials

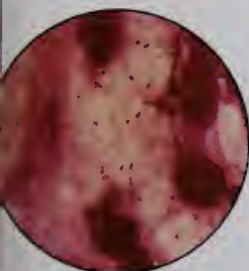
involving nearly 700 patients.<sup>10</sup> Overall clinical condition of the patients, changes in sputum purulence, reduction in sputum volume and microbiological clearance of pathogens—all improved more with Bactrim therapy than with tetracyclines. G.I. side effects occurred in only 7% of patients treated with Bactrim compared with 12% of tetracycline-treated patients. (See Adverse Reactions in summary of product information on next page.)

Bactrim is contraindicated in pregnancy at term and nursing mothers, infants under two months of age, documented megaloblastic anemia due to folate deficiency and hypersensitivity.

Bactrim DS. For acute exacerbations of chronic bronchitis in adults\* when it offers an advantage over single-agent antibacterials.

**References:** 1. Hughes DTD, Bye A, Hodder P: *Adv Antimicrob Antineoplastic Chemother* 112:1105-1106, 1971. 2. Jordan GW *et al*: *Can Med Assoc J* 112:91S-95S, Jun 14, 1975. 3. Beck H, Pechere JC: *Prog Antimicrob Anticancer Chemother* 1:663-667, 1969. 4. Quintiliani R: Microbiological and therapeutic considerations in exacerbations of chronic bronchitis, in *Chronic Bronchitis and Its Acute Exacerbations: Current Diagnostic and Therapeutic Concepts*; Princeton Junction, NJ, Communications Media for Education, Inc., 1980, pp. 9-12. 5. Schreiner A *et al*: *Infection* 6(2):54-56, 1978. 6. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 7. Chodosh S: Treatment of acute exacerbations of chronic bronchitis: results of a double-blind crossover clinical trial, in *Chronic Bronchitis and Its Acute Exacerbations: Current Diagnostic and Therapeutic Concepts*. *Op. cit.*, pp. 15-16. 8. Chervinsky P: Double-blind clinical comparisons between trimethoprim-sulfamethoxazole (Bactrim™) and ampicillin in the treatment of bronchitic exacerbations. *Ibid.*, pp. 17-18. 9. Dulfano MJ: Trimethoprim-sulfamethoxazole vs. ampicillin in the treatment of exacerbations of chronic bronchitis. *Ibid.*, pp. 19-20. 10. Medici TC: Trimethoprim-sulfamethoxazole (Bactrim™) in treating acute exacerbations of chronic bronchitis: summary of European clinical experience. *Ibid.*, pp. 13-14.

cks *H. influenzae*—even  
ampicillin-resistant strains



attacks *S. pneumoniae*



## Economical b.i.d.

# Bactrim™ DS

(160 mg trimethoprim and 800 mg sulfamethoxazole/Roche)

\*Due to susceptible organisms. Please see next page for summary of product information.

# Bactrim™

(trimethoprim and sulfamethoxazole/Roche)

Before prescribing, please consult complete product information, a summary of which follows:

**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. **Note:** The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections. **For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.** **For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.** **For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.**

**Also for the treatment of documented *Pneumocystis carinii* pneumonitis.**

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term; nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age.

**Warnings: BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL**

**PHARYNGITIS.** Clinical studies show that patients with group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hemopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions: General:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin, reassess coagulation time when administering Bactrim to these patients.

**Pregnancy:** Teratogenic Effects: Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folic acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea, pseudomembranous colitis and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarthritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage: Not recommended for infants less than two months of age.**

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

**Children:** Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

**For patients with renal impairment.** Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

**ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS:**

**Usual adult dosage.** 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 14 days.

**PNEUMOCYSTIS CARINII PNEUMONITIS:**

**Recommended dosage:** 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100, Tel-E-Dose® packages of 100; Prescription Paks of 20 and 28. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40. Pediatric Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); cherry flavored—bottles of 100 ml and 16 oz (1 pint). Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); fruit-licorice flavored—bottles of 16 oz (1 pint).

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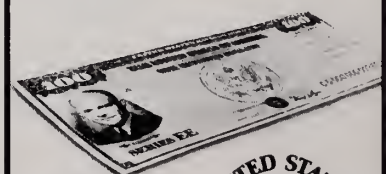
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# Fisiatría Pediátrica

Jesús A. Maldonado Hernández, M.D.

Es mi propósito al escribir este artículo el describir, en forma general, la fisiatría pediátrica, su importancia, métodos de tratamiento y sus diferencias con la fisiatría de adultos.

Al utilizar la frase niños impedidos, es muy común que la mayoría de las personas la asocien con condiciones como espina bífida, parálisis cerebral y distrofia muscular. Existen, sin embargo, otras condiciones (artritis reumatoidea juvenil, trauma a la médula espinal, accidentes cerebrovasculares, escoliosis, disfunción cerebral mínima y otros.) las cuales no son tan rápida ni tan fácilmente asociadas con este término pero que producen incapacidades físicas. Aún condiciones como las simples tortícolis congénitas y las frecuentes lesiones de plexo braquial pueden convertirse en incapacidad física si no son tratadas adecuadamente y a tiempo.

La niñez se caracteriza por ser un periodo de crecimiento y desarrollo tanto físico como emocional. La presencia de cualquier incapacidad física (no importa cuán leve y transitoria) produce un tremendo impacto familiar, social y emocional alterando el proceso de maduración, auto estima e interacción con el medio ambiente del niño. La mayoría de las incapacidades físicas en los niños ni son leves ni son transitorias. Lo más común es que permanezcan presentes a través de los años formativos extendiéndose hasta la vida adulta.<sup>1</sup>

La fisiatría pediátrica es una rama de la medicina de rehabilitación. Su meta es el desarrollo máximo del potencial residual de los niños y adolescentes con alteraciones del sistema neuro-musculoesquelético. A la misma vez le ofrece orientación a los padres sobre la condición y como manejarlo en su hogar. El propósito final de este proceso es promover la independencia y autoestima del niño para que su proceso de maduración sea lo más cercano posible a lo normal.

Muchas de las condiciones que ameritan un proceso de rehabilitación presentan aspectos en común (espasticidad, hipotonía, escoliosis, contracturas y otros). La diferencia entre estos aspectos estriba en su grado de severidad. Debido a esto dos niños que presenten el mismo diagnóstico ameritan prioridades diferentes y por tanto programas de tratamiento individualizado.

Los principios generales de tratamiento en la fisiatría pediátrica expuestos a continuación no se aplican por igual a todas las condiciones pero sirven para demostrar los propósitos generales al utilizarlos.

## Espasticidad

El aumento de tono muscular, producido al interrumpirse el control cortical, es uno de los mayores impedimentos de movilidad en un niño. Una vez presente no puede eliminarse

pero si modificarse. En su tratamiento se usan medicamentos, estimulación de antagonistas por diferentes métodos y posición de ciertas articulaciones. Ejemplo de esta última es la flexión de cadera y rodilla para disminuir el patrón extensor producido por la espasticidad en casos de parálisis cerebral. La complicación más temida de la espasticidad no tratada es el desarrollo de contracturas articulares. Estas se suman a la incapacidad ya existente haciendo de una extremidad con potencial funcional una con posibilidades mínimas o nulas de función (ejemplo, contractura del músculo gastrocnemio en un niño con diplegia espástica.)

## Contracturas Articulares

La posición prolongada de una articulación en un ángulo dado produce acortamiento de la cápsula articular, ligamentos y tejidos blandos periarticulares. Algunos factores que predisponen a el desarrollo de contracturas son: espasticidad, lesiones de nervios periféricos parciales o totales (lesiones de plexo braquial,) acortamiento muscular (tortícolis) y cambios inflamatorios agudos y crónicos (artritis reumatoidea juvenil). La presencia de contracturas en una extremidad produce serias consecuencias en la función y por ende en la independencia del niño. Un programa de ejercicios pasivos, adecuadamente delineado y aplicado, y la aplicación de férulas a estas articulaciones puede retardar, minimizar o evitar (según la condición) las contracturas y su efecto sobre la función.

## Escoliosis

Las causas de estas son múltiples: hipotonicidad, espasticidad asimétrica, desnivel pélvico y debilidad asimétrica entre otros.

El tratamiento tiene como meta el evitar el progreso de la curvatura dentro de lo posible. Para ello se utilizan accesorios para un sillón de ruedas, ortosis espinales y en casos más severos, la cirugía. El método de tratamiento dependerá de cada caso individual y de la severidad de la curva. La complicación más seria es el compromiso de la función cardiorespiratoria además de que una curvatura no tratada a tiempo dificulta el acomodar a un niño en la posición de sentado repercutiendo en su funcionalidad. El seguimiento frecuente de parte del médico y el instituir los medios adecuados a tiempo evitarán las complicaciones incapacitantes en estos niños.

## Ambulación

La independencia máxima en movilización en un ser humano la constituye la ambulación. La incertidumbre de si un niño lo logrará no, constituye una fuente de angustia para los padres. Lo mismo se aplica cuando en el pronóstico de una condición se vislumbra la pérdida de la ambulación (enfermedades neuromusculares).

En algunas condiciones neuromusculares es posible hacer un pronóstico de esta etapa pero en la mayoría de los casos no lo es. En estos casos se continúa el tratamiento y al llegar a las etapas inmediatamente anteriores a la ambulación el tratamiento médico debe ser más frecuente. De este momento en adelante se sucederán las consideraciones de equipos asistivos (andadores, bastones y muletas), abrazaderas y cirugía.

Los equipos asistivos tienen momentos adecuados e indicaciones precisas para utilizarse de acuerdo al desarrollo

alcanzado por el niño en determinadas etapas de la ambulación (una edad mental de dos a tres años se requiere para el uso de muletas)<sup>2</sup>.

La abrazaderas a ordenarse deben ser adecuadamente elegidas ya que al momento de utilizarse pueden resultar no funcionales. Esto puede ser debido a factores como peso, diseño y restricción inadecuada de ciertas articulaciones.

Antes de decidir sobre la cirugía de las extremidades inferiores los tratamientos conservadores deben ser ensayados. Otro factor a considerarse es que el alineamiento articular por cirugía o abrazadera en algunas ocasiones produce mayor incapacidad. Sin embargo, debemos tener en mente y no descartar, que en muchos casos el tratamiento más conservador es la cirugía misma.

### Ortosis

Bajo este término se incluyen todos aquellos aditamentos que se utilizan para proveer soporte a alguna parte del cuerpo con el propósito de mejorar función o evitar deformidades. Los principios ortóticos se aplican por igual a niños y adultos, pero las aplicaciones clínicas son diferentes.

A diferencia de los adultos, los niños presentan los factores de crecimiento y desarrollo los cuales al avanzar producen un elemento de cambio el cual, a su vez, actúa como fuerza dinámica<sup>3</sup>. Por esta razón nunca se deben seguir los parámetros establecidos de prescripción. Siempre se debe examinar al niño, observar la patomecánica envuelta y sumarlo a un conocimiento ortótico actualizado.<sup>3</sup>

No hay reglas escritas en cuanto a cuando ordenar una ortosis a un niño. La edad cronológica no es el mejor parámetro ya que en los niños con incapacidades ésta no corresponde siempre a su edad mental ni a su nivel de desarrollo. Este último sí puede tomarse como medida para ordenar una ortosis.<sup>2</sup>

- ¿Qué actividad hace el niño?
- ¿Cómo la ejecuta?
- ¿Cuál es la próxima actividad de desarrollo que este niño debería alcanzar?
- ¿Cuánto tardaría en adquirirla?

Por ejemplo, un niño que logra conseguir buen control de cabeza pero cuyo control de tronco no será alcanzado hasta un tiempo después necesita una ortosis espinal para alinear el tronco, mantenerlo en una posición adecuada para utilizar sus manos en otras actividades y adquirir una visión vertical del ambiente que le rodea.

Después de las consideraciones anteriores sigue la más crucial: la aceptación de la ortosis por el niño. La apariencia, contorno, diseño y peso de la ortosis, las actitudes de los padres, terapistas y médico son factores importantísimos en esta aceptación.<sup>3</sup>

Los nuevos plásticos y materiales disponibles junto a la gran variedad de diseño hacen del conocimiento ortótico actualizado una necesidad. Muchas de las ortosis que necesitamos pueden ser construidas por el terapeuta ocupacional en la oficina del médico (sobre todo, férulas para las extremidades superiores) mientras que otras deben ser ordenadas a un ortotista. En cualquier caso los conocimientos anatómicos y fisiológicos del médico son sumamente necesarios para que junto a estos profesionales se logre el aditamento más funcional para el niño.

### Sillas de Rueda

La importancia de estos sistemas es incalculable ya sea para uso temporero o para el niño con ambulación marginal o nula.

En los niños la movilización ocupa una primera prioridad ya que les permite desplazarse para explorar el medio ambiente y acercarse a los niños de su edad para participar más de cerca en sus actividades.

Estos sistemas no solo son para movilización, también permiten función por medio de la posición. La espasticidad, hipotonía y el desnivel pélvico promueven el desarrollo de escoliosis y kifosis. En la posición de sentado se trata de evitar estas complicaciones y se promueve la función.

En la selección de una silla de rueda para un niño hay que tomar en cuenta los siguientes factores:

- Edad
- Actividad
- Capacidad de autopropulsión
- Deformidades articulares y de la columna
- Hipertonía
- Hipotonía

Estos factores determinarán el tipo de silla y las modificaciones necesarias para un niño dado.

Existen en el comercio una gran variedad de estos sistemas, además de que en los últimos años los nuevos modelos se originan con gran rapidez. Esto tiende a producir un poco de confusión (aunque a la vez produce variedad).

- ¿Cuales de estos modelos son más funcionales para un niño o grupo de niños con incapacidades dadas?
- ¿Cuál es el mejor peso, la mejor configuración y qué accesorios se deben incluir?

Como ejemplo, podemos mencionar los sistemas Mullholland, MPI y Desesmo para la espasticidad. Para espina bífida y trauma a la médula espinal tenemos variedad de modelos convencionales y la reciente silla de rueda donde el niño se coloca de pie (Standing Wheelchair).

Aunque también la gama de accesorios para estos sistemas es amplia nos encontramos con casos en que los accesorios disponibles no cumplen su cometido en determinado niño. Si el médico sabe exactamente lo que necesita es muy fácil que esta modificación se construya conllevando mejor función al niño y economía a los padres.

Por último, tenemos el grupo de niños cuya espasticidad y deformidades les impiden sentarse en equipos convencionales. Hay gran variedad de soluciones individuales pero se necesita un ortotista con el entrenamiento y el equipo necesario para construirlos.

Recordemos que las prioridades al ordenar una silla de rueda son movilidad, alineamiento y función por el medio del sistema mas adecuado y con el menor número posible de accesorios.

### Estimulación del Desarrollo

Los programas establecidos y las técnicas desarrolladas en esta área para niños con incapacidades del desarrollo han provocado diversidad de opiniones. Los estudios llevados a cabo en esa área no han sido lo suficientemente prolongados para arrojar resultados concretos.<sup>4</sup> En adición las teorías des-



arrolladas para explicar su mecánica y efectividad son muy variadas<sup>4</sup> y vistas con escepticismo por muchos profesionales.

Aunque hablamos en este momento solo de incapacidades del desarrollo, estos programas (llamados de enriquecimiento) fueron originalmente organizados para incluir niños con factores de riesgo (bajo nivel socioeconómico, aislamiento ambiental, padres negligentes, prematuros y otros), inclusive han sido recomendados para niños normales con el propósito de acelerar su independencia y afinar sus destrezas.

En general, se trata de integrar el desarrollo de autosuficiencia física con las destrezas perceptuales, visuales y motoras y de comunicación. Se ayuda al niño a desarrollar en secuencia control de cabeza, posición de sentado, gateo, ponerse de pie y ambular estimulando conjuntamente su atención visual y auditiva y diferenciación sensorial. Por este medio se promueve en el niño pasar de una etapa de desarrollo desorganizado a una de coordinación y control corporal.<sup>5</sup>

Existen varias tácticas de estimulación sensorial y de neuromotor desarrollo (Bobath, Ayres, etc). Usualmente en el tratamiento de los niños se incorporan los aspectos positivos de varias técnicas. Sin embargo otras técnicas resultan muy complejas y extenuantes para los padres y su razonamiento científico no es considerado como convincente.

A pesar de las diferencias de opinión y técnicas, la estimulación del desarrollo es otra modalidad de tratamiento y es inseparable de la meta de función.

Cada etapa de desarrollo conlleva un aprendizaje dado para el niño. El hecho de un niño presentar un atraso (aun leve y sin hallazgos clínicos patológicos) en el desarrollo motor grueso implica un mayor tiempo en una etapa de aprendizaje que ya rindió su máximo. ¿Por qué no estimularlo a seguir con la próxima etapa de desarrollo? Según el ambiente en que crece el niño tiene repercusiones en su personalidad y comportamiento ulterior, ¿No sería posible que el atraso leve en el desarrollo motor tuviera repercusiones futuras en su personalidad y proceso de aprendizaje? ¿Le daría usted el beneficio de la duda?

### Electrodiagnóstico Pediátrico

Esta es una modalidad diagnóstica que incluye la electromiografía y el estudio de velocidad de conducción nerviosa. Las indicaciones usuales son debilidad o parálisis, dolor, parestias e hipotonías. Su utilidad consiste en confirmar, apoyar o descartar una impresión diagnóstica.

La aplicación de la técnica en el orden en que se hace en un adulto resulta difícil en un niño. La incomodidad de la aguja o corriente eléctrica produce un aumento en su actividad con el propósito de retirar la extremidad del estímulo. Estas reacciones predecibles pueden ser utilizadas para conseguir la actividad o inactividad que deseamos aunque esto conlleve una alteración del orden de la técnica habitual.

En los primeros meses de vida los músculos mas distales no están activos y estos pueden explorarse primero evitando así la interferencia de la contracción.<sup>6</sup> También podemos aprovechar los reflejos primitivos presentes para conseguir contracción o relajación de grupos musculares dados.

En cuanto a los resultados que podemos obtener del estudio hay diversidad de factores a considerar. Entre estos se encuentra el proceso incompleto de mielinización de los nervios periféricos lo cual nos provee valores diferentes a los del adulto, pero que son normales en niños de determinadas edades.<sup>7, 8</sup> También el porcentaje de músculo fetal es alto en las primeras semanas de nacido. Por estas razones la interpreta-

ción de estas pruebas pueden ser completamente erróneas si no se tienen conocimientos de las características fisiológicas del sistema neuromuscular del niño.

El electrodiagnóstico también nos ayuda a planificar y reestructurar metas y planes de tratamiento. Por ejemplo, en lesiones de nervios periféricos la re-inervación se manifiesta eléctricamente antes de clínicamente, por lo tanto nos podemos adelantar a las próximas funciones que adquirirá el niño y encaminar el proceso del tratamiento en esa dirección.

Es imposible cubrir todos los aspectos de la fisiología pediátrica en este artículo. Posiblemente en otra ocasión pueda brindarle información más detallada de los aspectos aquí mencionados y de los que no se pudieron discutir.

Antes de terminar, sin embargo, quisiera escribir algunas palabras sobre el elemento más importante alrededor del cual gira el tratamiento del niño: *los padres*.

La orientación a los padres sobre la condición del niño y qué se puede hacer por él es vital. Los sentimientos de culpa, angustia, desesperanza e importancia son sumamente incapacitantes y si no se les trabaja a tiempo generarán actitudes perjudiciales al niño. A la misma vez, estos mismos sentimientos mueven a los padres, en muchos casos, a buscar soluciones y alternativas a su situación dirigiéndose al médico. Si los padres no son adecuadamente dirigidos, corren el peligro de caer en la multitud de servicios fragmentados existentes, los cuales a veces producen solo un bien a medias, llevando a una funcionalidad parcial. El programa de tratamiento debe ser lo más integro posible teniendo a los padres como parte integral y activa. De esta forma disminuimos su sentido de impotencia y aprenden a manejar la incapacidad de su niño con un mínimo de temor.

Con el manejo adecuado podemos integrar al niño impedido proveyéndole un lugar valioso en su futuro y en nuestra sociedad.

**Resumen:** El artículo comienza mencionando las condiciones más frecuentes que padecen los niños impedidos seguido del impacto que produce una incapacidad en todos los aspectos de su vida. Se define la Fisiología Pediátrica en base a sus metas. Se mencionan las manifestaciones más comunes de las enfermedades neuromusculares para luego describir, en forma general su manejo.

Las modalidades más comunes de tratamiento en la Fisiología Pediátrica se discuten en términos de aplicaciones generales. Termina el artículo enfatizando el papel de los padres dentro del manejo de la rehabilitación del niño.

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# Diagnóstico y Tratamiento de la Diabetes Infantil

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La diabetes sacarina en niños es una enfermedad peculiar por sus características, sus formas de presentación, su evolución a corto y largo plazo, los objetivos y los problemas de su tratamiento.

La diabetes es menos frecuente en niños, pero suele ser de presentación más abrupta, y de no diagnosticarse y ser tratada a tiempo puede dar lugar a consecuencias fatales. La mayor parte de los niños diabéticos son insulín dependientes, siendo raras las otras formas de diabetes. En ellos, el factor ambiental parece jugar un papel de importancia en la etiopatogenia de la condición. En ellos solo suelen encontrarse con más frecuencia ciertos haplotipos de HLA específicos que servirán de marcadores genéticos de la condición.

Evaluable el tipo de intolerancia a los carbohidratos entre los pacientes evaluados y tratados en nuestro consultorio en los últimos cuatro meses, y en los cuales el diagnóstico se hizo antes de los 20 años de edad, encontramos:

TABLA I

Intolerancia a los Carbohidratos y Diabetes Mellitus			
Anom. Cho	Todos	Hembras	Varones
TIPO I	47/57 82.46%	20/23 86.96%	27/34 78.41%
TIPO II	3/57 5.26%	2/23 8.27%	1/34 2.94%
A.P.T.G.	7/57 12.28%	1/23 4.25%	6/34 17.65%

Anom. Cho: Anomalia Carbohidratos

Int. Cho: Intolerancia Carbohidratos

A.P.T.G.: Anomalia Previa Tolerancia a Glucosa

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Trabajo presentado en las VIII Jornadas Diabetológicas de la Cruz Roja Española - Marzo 1983, Madrid, España.

La condición puede manifestarse a cualquier edad. En los niños predomina la Diabetes tipo 1 (insulín dependiente), como observamos en la tabla anterior de nuestra casuística. Los pacientes con Intolerancia a los Carbohidratos que hemos seguido han mantenido una condición estable sin progresar a una diabetes franca, o bien han retrocedido, reclasificándose como Anomalia Previa a la Tolerancia a la Glucosa. Ello parece indicar que se trata de otro grupo distinto de pacientes o de enfermedad diferente al tipo 1. El grado de intolerancia inicial a los carbohidratos (hiperglicemia) parece ser un leve índice pronóstico de la condición, aunque por el bajo número de pacientes aquí estudiados no nos atrevemos a darlo por definitivo.

La diabetes tipo 1 afecta a ambos sexos por igual. Por razones inexplicables en nuestra serie se observa un mayor número de sujetos varones, como se observa en la siguiente figura:

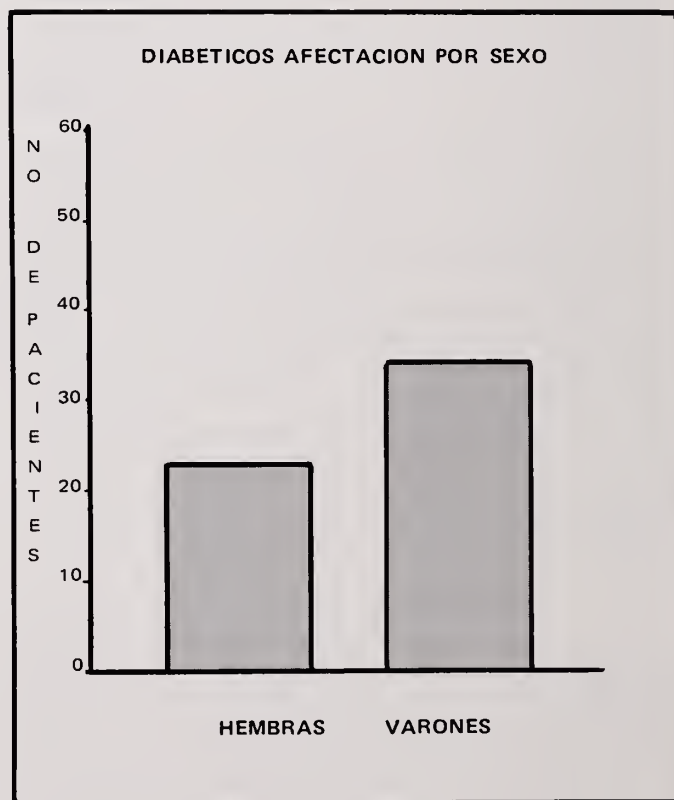


Figura 1

## Intolerancia a Carbohidratos y Diabetes Afectación por Sexo

Pretendemos estudiar en un futuro, otros pacientes de la misma edad, al igual que de otras edades, con la misma condición, que no fueron incluidos por la premura de los datos, para así analizar más detalladamente este aspecto.

En nuestro estudio documentamos como diagnósticos asociados en los 57 pacientes diversas condiciones entre las que destacan la obesidad, lesiones de lipoatrofia e hipertrofia, además de enfermedades tiroideas, como se observa en la siguiente tabla:



TABLA II

Diagnósticos Asociados	
Obesidad	7
Lipoatrofia	5
Lipohipertrofia	2
Hipoglicemia	2
Hipertiroidismo	1
Hipotiroidismo	1
Estatura Corta	1
Psicosis	1
Vitiligo	1
Micosis Cutanea	1
Telarquia Prematura	1
Sind. Genesis Caudal	1
Embarazo Gemelar	1

### Sintomatología

Con frecuencia, la condición comienza y se manifiesta en épocas específicas del año, las cuales suelen ser similares a épocas estacionales específicas en los distintos hemisferios, lo que favorece la presencia de algún factor ambiental, probablemente infecciones virales, como factor desencadenante de importancia a los así genéticamente susceptibles.

En nuestro medio, la condición suele manifestarse en los meses de enero y febrero, noviembre y diciembre, con un pico intermedio en mayo y junio. En los meses de julio y agosto, cuando existe el periodo de vacaciones escolares de verano, la presentación de casos nuevos suele ser muy baja (ver figura).

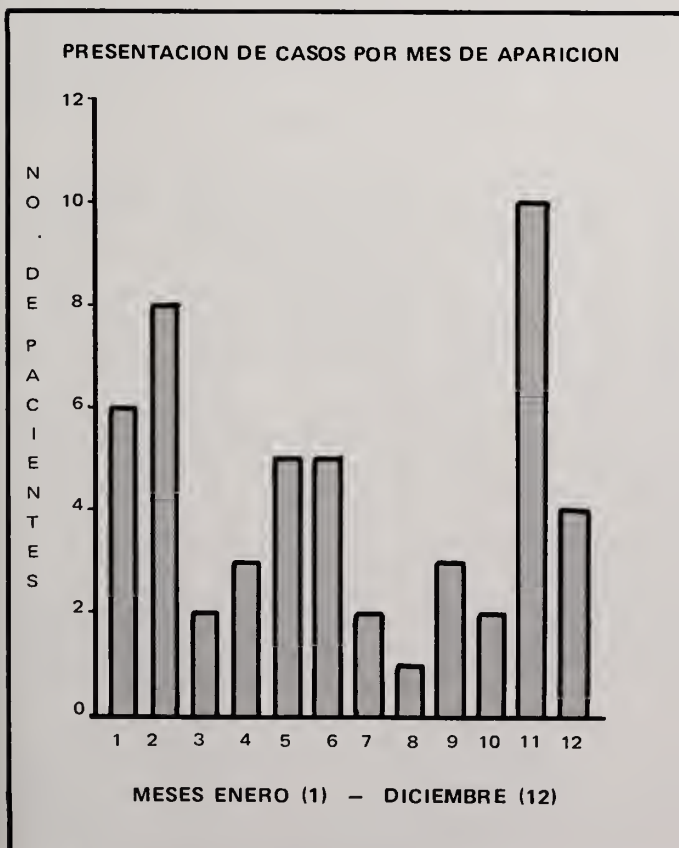


Figura 2

Se observó una mayor presentación de casos nuevos en los años 1975, 1979, y 1981 - 82 (figura 3).

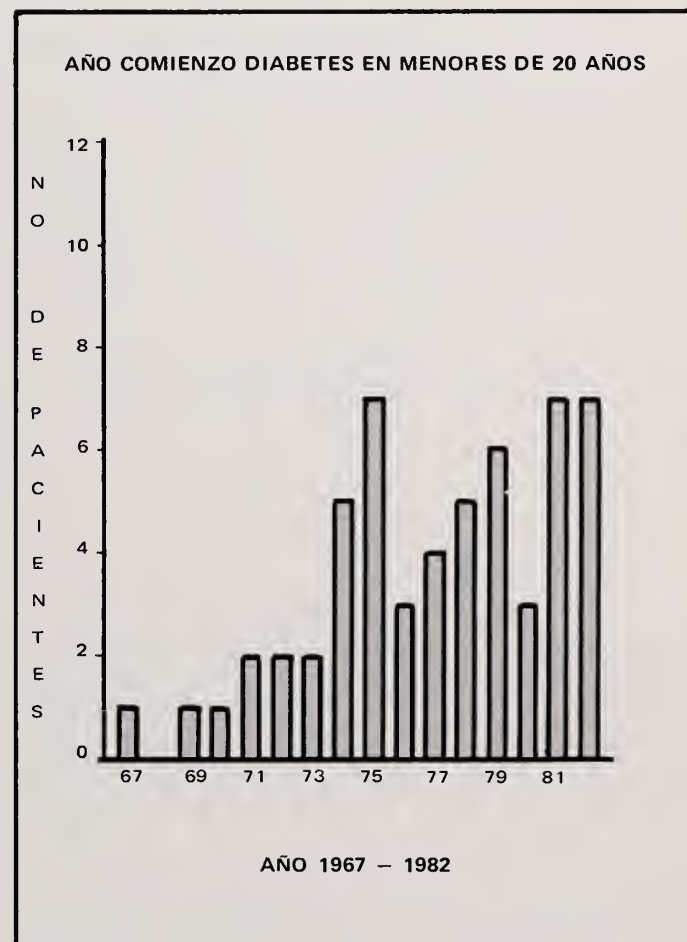


Figura 3

El niño suele presentar signos y síntomas evidentes a los padres, los maestros, los vecinos y a otros, tempranamente al comienzo de la condición. Además de los signos y síntomas clásicos, el niño puede cambiar su comportamiento convirtiéndose en un niño conflictivo o comenzar a tener problemas de aprendizaje.

Los maestros suelen notar que el niño sale mucho del aula de clases a beber agua o ir al baño, disminuye su capacidad de aprendizaje, disminuye su agudeza visual, especialmente para leer la pizarra, se torna irritable y disminuye su capacidad de atención, se muestra somnoliento (en esta fase puede perder el apetito y presentar náuseas y vómitos), además de disminuir su ejecutoria atlética debido al agotamiento y la fatiga.

El que el personal escolar conozca los detalles de la enfermedad permitirá una detección más temprana, a la vez que facilitará grandemente el tratamiento del niño, además de su adaptación futura a la condición. Consideramos una responsabilidad social del Estado el que en los programas preparatorios de los maestros se les requiera a éstos una formación diabetológica.

El comienzo es variable, aunque suele evolucionar en una forma más rápida que en los adultos, al igual que predomina la desnutrición o el peso normal, en lugar de obesidad que es

más frecuente en la Diabetes tipo 2 (no-insulinodependiente), que predomina en el adulto. Los hallazgos clínicos están directamente relacionados con la duración y el grado de deficiencia insulínica.<sup>1</sup>

La presentación de síntomas puede variar de uno a dos días hasta varios meses antes de la presentación de la acidosis, aunque en la mayor parte de los casos suele ser menor de un mes de duración. En nuestro grupo recientemente estudiado, encontramos que el diagnóstico se hizo a los 19 días de comenzada la sintomatología, lo que implica un diagnóstico bastante temprano por nuestros pediatras, comparado con los datos de otras clínicas, como son los de P. White en la Clínica Joslin de Boston, donde se observó una sintomatología de una duración mayor de un mes al momento de hacerse el diagnóstico.<sup>2</sup>

TABLA III

Días Síntomas al hacer el Diagnóstico			
Todos	19.37	N = 43	11?
Varones	21.78	N = 23	8?
Hembras	16.6	N = 20	3?

En ocasiones, puede existir desde varios años antes del comienzo de los síntomas, un historial de hipoglicemias espontáneas como un hallazgo aislado. En nuestra experiencia, hemos evaluado dos niños con un episodio convulsivo secundario a hipoglicemia asociada a Intolerancia a los Carbohidratos. Con frecuencia aparece un historial de glucosuria transitoria, a la cual injustificadamente suele dársele, en ocasiones, poca importancia, estando asociada a períodos de stress, o de hiperalimentación.

La poliuria y la polidipsia representan los síntomas de presentación más frecuentes, encontrándose en aproximadamente un 75% de los casos.<sup>3</sup> La nicturia, polifagia, astenia, y la disminución de peso están presentes en un 40—50% de los casos.<sup>3</sup> En nuestra experiencia hemos observado:

Tabla IV

	Sintomatología al Inicio		
	Todos	Hembras	Varones
Polidipsia	76.79%	86.96%	67.70%
Poliuria	78.57%	86.96%	72.73%
Polifagia	33.93%	34.78%	30.30%
Anorexia	30.36%	34.78%	27.27%
Disminución de peso	64.29%	69.56%	60.60%
Enuresis	21.43%	26.09%	15.15%
Infecciones	12.5%	8.7%	15.15%
N	56	23	33

Resalta en estos pacientes la frecuencia relativa de anorexia en un 30% de los mismos, hallazgo que contrasta con lo encontrado en los adultos, presentando los niños una polidipsia marcada, a la vez que rechazan los alimentos sólidos. Este hecho fue observado por nosotros en un estudio previo en 1972,<sup>4</sup> habiendo sido informado también por otros autores como Callamand, en Colombia y Guell, en Cuba.<sup>5 6</sup>

Al profundizar en el historial, se observa con frecuencia hipertriosis, prurito, piel reseca, infecciones cutáneas, mayormente del tipo de intertrigo o infecciones secundarias en las áreas genitales de los niños pequeños. Con cierta frecuencia encontramos factores descompensadores como infecciones (mayormente respiratorias), trauma o stress emocionales. En las niñas hemos observado una baja incidencia de infecciones vaginales.

Una vez instaurado el cuadro de diabetes manifiesta, este es progresivo, si no se trata adecuadamente. El individuo susceptible comienza a presentar manifestaciones metabólicas subclínicas, que evolucionan a una fase química y finalmente a la diabetes clínica manifiesta. El paso de una fase a otra es muy variable. Hasta los trabajos de Cudworth y colaboradores se pensaba que el paso de descompensación en la diabetes tipo 1 era abrupto, pero este autor pudo demostrar, con el seguimiento de un sujeto con haplotipos de riesgo y con familiares inmediatos insulinodependientes, que el tiempo transcurrido desde la presencia de anticuerpos antiisletos hasta la fase clínica puede transcurrir hasta en año y medio, lo que constituye un periodo no muy corto.<sup>7</sup> Estos hallazgos, junto con avances en inmunología quizás permitan prevenir el progreso de la condición en algunos sujetos a riesgo en un futuro.

A medida que la habilidad diagnóstica de los médicos y las facilidades de laboratorio han mejorado, la presentación de cetoacidosis y coma en el momento de la primera evaluación médica ha disminuido grandemente. Por ello, de un 52% informado por Jackson y colaboradores en 1949<sup>8</sup> encontramos cifras en años posteriores de 18 y 20%<sup>9 10</sup>. En el grupo recientemente revisado por nosotros, ninguno llegó en coma al hospital.

Los vómitos con disminución de la ingesta representan un signo ominoso que conlleva a un coma cetoacidótico rápidamente. Cuando sobreviene una acidosis moderada ( $< 15\text{mM/L}$  de  $\text{CO}_2$ ) comienza a presentarse una respiración profunda y rápida, la cual se convertirá en la típica respiración de Kussmaul al presentarse una acidosis metabólica severa ( $< 10\text{mM/L}$  de  $\text{CO}_2$ ). El pH plasmático puede descender, incluso, hasta valores de 6.85 a 7.00.

Los signos de deshidratación no son obvios hasta que se ha producido una pérdida del 5% del peso corporal. Cuando el comienzo es insidioso, predomina entonces la malnutrición, no pudiéndose tener en cuenta la pérdida de peso para determinar el grado de deshidratación exacta. Cuando es severa (15%) hay signos de insuficiencia circulatoria.

El estado precomatoso se caracteriza por estupor o somnolencia, sequedad de piel, mejillas rubicundas, labios sonrosados, feto cetónico, hiperpnea, náusea y vómitos, y, en ocasiones, dolor abdominal o dolorimiento corporal generalizado.

En la fase comatosa observamos la respiración de Kussmaul, ojos hundidos y de bajo tono, dolorimiento abdominal difuso o generalizado a la palpación, pulso rápido y débil, y una tensión arterial subnormal. Si hay un factor infeccioso descompensador, encontraremos los signos y síntomas de éste.



El coma cetoacidótico adecuadamente tratado presenta en estos momentos una mortalidad baja. Con el diagnóstico precoz, los adelantos terapéuticos e instrumentales del momento deberá disminuirse a cifras ínfimas menores al 1%.

La recaída a largo plazo de los periodos cetoacidóticos van en relación directa con el grado de educación diabetológica del paciente y sus familiares; a mejor comunicación y educación de parte de los profesionales de la salud, menor es la incidencia de las recaídas y etapas de descompensación, que si se descuidan pueden ser más frecuentes en los primeros cinco años de la enfermedad y durante la adolescencia por peculiaridades de cambio de carácter y de aceptación de la enfermedad en este período.

### Cambios Químicos y Diagnóstico

La glicosuria e hiperglicemia con o sin cetonuria son diagnósticos de diabetes manifiesta. La ausencia de hiperglicemia en ayunas no descarta la posibilidad de la enfermedad. La rapidez de progresión de la intolerancia a los glúcidos a cetoacidosis es impredecible, por ello se recomienda un seguimiento médico adecuado una vez que se sospecha el diagnóstico.

Puede existir cetonuria sin anomalías marcadas en el equilibrio ácido-base, no existiendo relación consistente entre el grado de hiperglicemia y cetonuria.

En la fase de descompensación acidótica el colesterol, los lípidos totales, el nitrógeno ureico, y la hormona de crecimiento suelen estar incrementados. El pH sanguíneo y el CO<sub>2</sub> disminuyen. En la orina, puede encontrarse proteínas y cilindros, los cuales desaparecerán al corregirse la acidosis y la deshidratación. En sangre periférica puede observarse hemoconcentración y leucocitosis con desviación a la izquierda. La hiperlipemia puede dar lugar a una hiponatremia relativa. Inicialmente el potasio sérico suele ser normal o algo elevado, a pesar de que el potasio corporal está disminuido.

Siempre que se encuentre azúcar en la orina, el paciente debe ser evaluado con una glicemia. De ser normal debe procederse a realizar una prueba de sobrecarga oral además de tratar de identificar el tipo de azúcar presente en la misma. Si hay cetonuria asociada a la glicosuria, se debe determinar la glicemia inmediatamente.

La glicosuria y la hiperglicemia al azar son manifestaciones tardías de la diabetes mellitus. Al igual que en otras endocrinopatías existen pruebas para calibrar la capacidad secretora de la glándula afecta. Entre ellas podemos citar: la tolerancia o sobrecarga de glucosa oral o endovenosa, tolerancia de cortisona, prueba de glucagon y tolbutamida, y determinaciones de insulina en relación con los niveles de glicemia.

De las pruebas provocativas la más utilizada es la prueba de sobrecarga oral. Para ella seguimos los criterios del Grupo Internacional que estableció hace tres años las nuevas bases y clasificación de la diabetes, con dicho grupo colaboramos en establecer los criterios para el diagnóstico de la diabetes en niños.<sup>11 12</sup>

Toda glicemia plasmática en ayunas mayor de 115 mgr.% nos debe hacer sospechar intolerancia a los carbohidratos. Si dicha glicemia es superior a los 140 mgr.%, y es confirmada, nos hará sospechar diabetes, la cual ha de ser confirmada con otras glicemias. Si la glicemia en ayunas es mayor de 115 pero inferior a 140 mgr.% nos dará el diagnós-

tico de Intolerancia a los Carbohidratos. Valores superiores a los 200 mgr.% en el periodo de 0 a 2 horas en una prueba de tolerancia serán indicativos de diabetes. Aquellos valores intermedios entre 140 a 200 mgr.% serán indicativos de Intolerancia a los Carbohidratos.

Para realizar la prueba de sobrecarga en niños hay que ajustar la cantidad de glucosa a administrar a 1.75 Gm./kg. de peso ideal. El paciente habrá de tener un ayuno de 8 a 16 horas y estar en reposo en el laboratorio. Habrá de tener una ingesta adecuada de carbohidratos de por lo menos 150 Gm./día los tres días previos a la prueba. Obviamente, se debe conocer el método de análisis de sangre (plasma, sangre total, etc.) por las correcciones pertinentes que han de hacerse.

En ningún niño estará justificado el realizar determinaciones de sobrecarga oral a no ser que presente una clínica que haga sospechar la condición.

### Otras Formas de Diabetes e Intolerancia a Carbohidratos en Niños

#### Diabetes No Insulinodependiente o Diabetes Tipo 2

La diabetes tipo 2, antiguamente conocida como Diabetes Estable o tipo adulto, es de rara presentación en niños. Generalmente se observa en niños obesos y usualmente asintomáticos. Las manifestaciones clínicas, si están presentes, suelen ser leves. Se sospecha el diagnóstico debido a obesidad e historial familiar de diabetes y debido a glicosuria.

La tolerancia a la glucosa es anormal y la respuesta insulínica es similar a la de los diabéticos obesos adultos. Responden a hipoglicemiantes orales, pero en ellos se ha de emplear inicialmente, y si es posible en todo momento, como tratamiento único, una dieta de restricción calórica adecuada. Con frecuencia, al llegar a su peso ideal la intolerancia a los carbohidratos vuelve a lo normal, o mantiene valores de glicemia aceptables.

#### Diabetes Transitoria del Recién Nacido y de la Infancia

Suele presentarse como un cuadro transitorio de hiperglicemia (en el R.N. implica todo valor superior a 125 mgr.% tras un ayuno de 4 horas) cuya aparición tiene lugar en las primeras seis semanas de vida. Es sensible a la insulina y no se asocia a la cetosis.<sup>13</sup> De forma característica hay hiperglicemia, glicosuria y deshidratación.

Ramsey<sup>14</sup> informó en 1926 el primer caso de la enfermedad, quien veinticinco años después era completamente normal. La condición es extremadamente rara, existiendo pocos casos informados en la literatura.

Múltiples causas han sido postuladas, entre ellas, desbalance hipotalámico transitorio, infección, trastornos adrenocorticales e hipoinsulinismo secundario a hipoplasia de las células beta.<sup>13</sup>

Nosotros hemos visto un solo caso, el cual fue dado de alta de nuestra sala de recién nacidos al mes de edad en franca recuperación de su condición, con niveles estables de su glicemia. Cinco años después desconocemos el paradero y la condición del niño el cual no volvió a seguimiento.

### Manifestaciones Clínicas

Se presenta usualmente en niños de bajo peso al nacer, afectando ambos sexos por igual. Suelen presentar deshidratación y emaciación marcada, con ausencia de vómitos y diarrea, pero sí con poliuria. Se observa una palidez peculiar, facies "alerta" con ojos abiertos y cierta apariencia de "niños mayores". La grasa subcutánea es mínima y raramente hay evidencia de infección.

Los casos informados nunca han presentado cetosis marcada, habiéndose observado cetonuria en muy pocos casos<sup>15 16</sup>. Suelen ser sensibles a la insulina, siendo el cuadro clínico usualmente corto y de rápida respuesta a la terapia.

La duración de la hiperglicemia es variable. La glicosuria, entre los casos informados, persistió en uno,<sup>17</sup> o desapareció en 3 a 14 días en otros cuatro.<sup>15 17 19</sup>

La enfermedad puede confundirse fácilmente con hiperplasia adrenal congénita y con galactosemia, las cuales se deben incluir en el diagnóstico diferencial, al igual que la diabetes mellitus permanente del recién nacido e infante.

Una vez que la hiperglicemia y la glucosuria se corrigen, la tolerancia a la glucosa suele ser normal. De los casos informados cinco pacientes han sido seguidos por un periodo de tres a veinticinco años y continúan siendo normales.<sup>13</sup>

### Terapia

La terapia estará encaminada a controlar la hiperglicemia, la hipertonicidad y la deshidratación asociada. La insulina se utilizará a dosis muy bajas, vigilando muy de cerca su efecto debido a su alta sensibilidad a la misma. Si la glicemia sobrepasa los 300 mgr.% se precisarán líquidos endovenosos. Inicialmente se empleará una solución hipotónica sin glucosa (120 meq./L de sodio; 4/5 de Ringer + 1/5 de agua) en cantidad de 60 a 80 ml./Kg. en las primeras 12 horas o hasta que la glucosa alcance valores de 300 mgr.%. Luego se añadirá una solución glucosada al 5% en cantidad de 150 a 200 ml./Kg./día.

### Diabetes Mellitus Permanente del Recién Nacido e Infante

Sólo puede diferenciarse de la forma transitoria por su curso y por su mayor tendencia a la cetoacidosis. El caso más joven informado en la literatura, fue una niña de 60 horas de edad.<sup>20</sup> Se trata de una condición extremadamente rara.<sup>20-28</sup>

### Diabetes Lipoatrófica

Constituye una condición rara donde se asocian lipoatrofia total o parcial, hipertrofia fática y muscular, hepatomegalia, hiperlipemia y diabetes resistente. Usualmente la hiperglicemia es no cetósica y resistente a la insulina. Se ha encontrado además, hiperinsulinismo, hiperproteinemia, y cifras elevadas de hormona de crecimiento.

Existe una forma parcial de la cual se han descrito más de 200 casos, y una forma total mucho más rara. Nosotros hemos tenido la experiencia en nuestro medio de evaluar un paciente con manifestaciones somáticas de la condición, con resistencia a la insulina, pero con un cuadro químico incompleto.

Se postula una herencia autosómica recesiva, descubriéndose algunos casos con retardo mental<sup>29</sup> con manifestaciones somáticas de la condición, con resistencia a la

insulina, pero con un cuadro químico incompleto.

Se postula una herencia autosómica recesiva, descubriéndose algunos casos con retardo mental.<sup>29</sup>

### Coma Hipersomolar no Cetosico en Niños

Se trata de un complejo síndrome extremadamente raro en niños, que se caracteriza por hiperglicemia marcada e hiperosmolaridad, deshidratación severa, coma, y escasa o ninguna acidosis. Tienden a ser muy sensibles a la insulina, y en ellos hay que emplear solución salina 1/2 Normal, es decir hipotónica. La mortalidad es muy alta, aproximándose al 50% en casi todas las series.<sup>30</sup>

### Diabetes Asociadas a Otros Procesos en Niños

Suelen ocurrir cuando se producen en exceso hormonas antagonistas de la insulina e hiperglicemiantes. Tal es el caso de los hiperadrenocorticismos (primarios o secundarios), hipertiroidismo, gigantismo, y feocromocitomas. Raramente dan un cuadro clínico manifiesto de diabetes, siendo mayormente ejemplos de fases latentes o químicas en la evolución de la enfermedad.

La malnutrición y las tesaurosismos glucogénicas pueden producir intolerancia por los glicidos. En el síndrome de Prader Willi la diabetes suele ser secundaria a trastornos hipotalámicos.

### Diagnóstico Diferencial

Los niños en los cuales se considera el diagnóstico de diabetes mellitus se pueden agrupar artificiosamente en tres grupos:

1. historial sugestivo,
2. manifestaciones clínicas de acidosis con o sin estupor y coma,
3. glucosuria,
4. glucosuria transitoria o permanente.

En todos, el diagnóstico depende de los datos de laboratorio. Es necesario, sin embargo, descartar las formas secundarias (hipercorticismos, hipertiroidismo, etc.). La glicosuria transitoria puede ser secundaria a hiperalimentación (glicosuria alimenticia), infecciones agudas, infecciones y lesiones cerebrales, intoxicación por plomo y ciertas drogas como tetraciclina y sus productos de degradación. Los salicilatos pueden reducir la solución de Benedict, dando valores falsos. En la glicosuria renal, usualmente hereditaria, debido a un dintel renal bajo para la glucosa, no se observa hiperglicemia.

Resulta importante el recordar que no todos los azúcares en la orina son glucosa, teniendo que descartar pentosurias y galactosemia, especialmente en niños pequeños. De aquí la importancia de los métodos que utilizan la glucosa oxidada para la determinación de glucosa en la orina. Puede existir glucosuria renal por enfermedad tubular como se observa en el síndrome de Fanconi, o por daño tubular secundario a plomo o a productos de degradación de las tetraciclinas.

Se deben descartar todas las causas de coma, como son hipoglicémico, urémico, hepático, por hemorragia cerebral e intoxicaciones.

**La segunda parte de este artículo, donde se discute el tratamiento de la Diabetes Infantil será publicado en el próximo número del Boletín.**



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## AGRADECIMIENTO

La utilización de papel cromado de alta calidad para la publicación de este número del Boletín de la Asociación Médica de Puerto Rico ha sido posible gracias a una donación de la Sección de Pediatría de la Asociación Médica.

La Junta Editora del Boletín de la Asociación Médica de Puerto Rico le da las gracias por este medio a la Directiva de la Sección. Su aportación ha hecho posible lograr la excelencia gráfica que nuestro órgano oficial se merece.

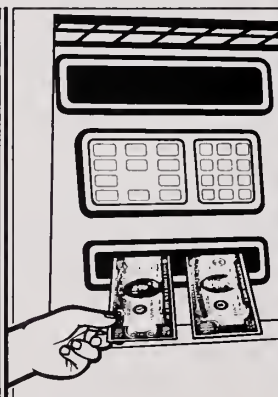
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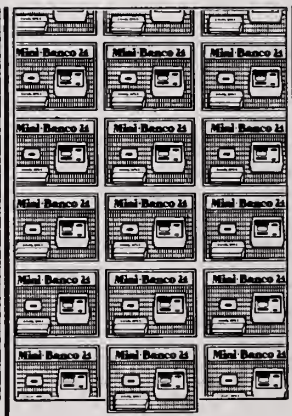
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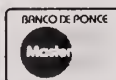
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# Presentación de Casos

## Cystic Fibrosis of the Pancreas Presenting as Metabolic Alkalosis

Aurea I. Muñoz, M.D.  
Anali Rodríguez, M.D.  
Juan F. Jiménez, M.D.

**Abstract:** A 5 month-old infant with cystic fibrosis who presented with salt depletion, metabolic alkalosis, and failure to thrive is described. Possible mechanisms responsible for these findings are discussed. The importance of considering cystic fibrosis as a diagnostic possibility in infants with such manifestations is stressed.

The serum electrolytes are usually normal in patients with cystic fibrosis (CF); however, previous reports have described the occurrence of salt depletion and metabolic alkalosis in association with this disease.<sup>1 2</sup> This paper describes our experience with an infant who presented the above disturbances as an early manifestation of cystic fibrosis.

### Case Report

AOG, a female infant, was born uneventfully at term, weighing 7 lbs 10 oz. She was first admitted to the San Juan City Hospital on 12/29/80, at age 3 months, with bronchopneumonia. History, though poorly reliable, revealed serious socioeconomic problems and an inadequate diet. The baby was removed from the hospital after 48 hours against medical advice. She remained in apparent good health until age 5 mos, when she was readmitted with the diagnoses of severe malnutrition and underdevelopment, clinical sepsis and dehydration. There was no history of antecedent abnormal gastrointestinal losses but there had been diminished intake during the preceding two weeks. Physical examination revealed opisthotonos, bulging fontanel, and moderate hepatomegaly. Vital signs were normal and no foci of infec-

tion were evident, pertinent laboratory data included the following urinary findings: specific gravity 1.022, pH 6, protein traces, acetone 1+, and a normal sediment. Chest film was negative. Lumbar puncture, subdural tap and CT scan of brain were nonrevealing, as were tests for reducing substances and amino acids in urine. SGOT was 121 U/L, SGPT 83 U/L, total serum protein 4.1 gm/dL, serum albumin 2.0 gm/dL, serum bilirubin 1.3 mg/dL, LDH 549 U/L, BUN 9 mg/dL, serum creatinine 0.5 mg/dL. Liver biopsy showed severe steatosis and mild cholestatic changes. There was no visualization of the gallbladder on abdominal sonography. Initial serum electrolyte findings in mEq/L were as follows: Na 120, K 2.7, Cl 74, HCO<sub>3</sub> 36.5. Arterial blood pH was 7.65, pCO<sub>2</sub> 36 mm Hg, pO<sub>2</sub> 121 mm Hg. Similar abnormal results were obtained on several determinations during the first 36 hours of intravenous fluid therapy, restoration of normal fluid and electrolyte balance ensuing thereafter. (Chart review of the previous admission disclosed the following values: Na 124 mEq/L, K 3.8 mEq/L, Cl 81 mEq/L, HCO<sub>3</sub> 34 mEq/L, arterial blood pH 7.5). Sweat chloride determinations were 90 and 88 mEq/L, respectively. Quantitative analysis of stool trypsin and chymotrypsin revealed normal values. Measurement of stool fat was not possible due to technical difficulties. The patient remained in the hospital for two months, receiving antibiotic and supportive therapy, and gaining one pound of weight in that interval. There were no abnormal respiratory or gastrointestinal manifestations during her stay.

One month after discharge, having been lost to follow-up, the patient was readmitted with moderately severe dehydration and in respiratory distress. Chest film showed extensive pneumonic changes. Serum electrolyte findings on admission (mEq/L) were Na 120, K 1.8, Cl 66, HCO<sub>3</sub> 40, with a blood pH of 7.48. Blood culture yielded *Escherichia coli*, and a subsequent tracheal aspirate grew *Pseudomonas aeruginosa*. As the patient's condition worsened, a mixed type of acidosis supervened, and death occurred six days after admission. Postmortem findings confirmed the diagnosis of cystic fibrosis, also revealing extensive pneumonia with abscess formation, hepatic steatosis, and mild portal fibrosis.

### Discussion

Though classically associated with respiratory and gastrointestinal manifestations, a wide variety of signs and symptoms can be presenting findings in cystic fibrosis (Table I). Initially, this patient posed a diagnostic dilemma because of the complexity of her clinical picture. Despite the absence of pulmonary or gastrointestinal symptoms at the time, the diagnosis was suspected because of the persistent hypoelectrolytemia and metabolic alkalosis. These chemical findings are infrequent in infancy, being seen more commonly in pyloric stenosis and other forms of intractable vomiting. Less frequent causes of metabolic alkalosis are listed in Table II.

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*Presented in part at the Annual Meeting of the P.R. Medical Association, November, 1982.*

TABLE I

Cystic Fibrosis of Pancreas Possible Presenting Findings
Episodes of pneumonia
Bronchiectasis
Recurrent cough and / or wheezing
Meconium ileus
Sinusitis
G-I manifestations (loose stools, steatorrhea, pancreatitis)
Failure to thrive
Nasal polyps
Rectal prolapse
Infertility
Increased intracranial pressure
Metabolic alkalosis

TABLE II

Causes of Metabolic Alkalosis in Infancy
Intractable vomiting (pyloric stenosis, others)
Unreplaced losses from gastric drainage
Chloride-losing diarrhea (familial)
Potassium-losing nephropathy
Chlorothiazide diuresis
Administration of alkali solutions
Bartter's syndrome
Excessive glucocorticoids
Metabolic compensation for respiratory acidosis
Cystic fibrosis

As previously stated, electrolyte depletion with metabolic alkalosis has been described in patients with CF, particularly during summer months and in arid climates. There may be heat prostration, with extreme dehydration, vascular collapse and hyperpyrexia, or less severe dehydration due to chronic gradual losses. The latter type of presentation may be the initial manifestation of the disease, and usually occurs in infants less than 12 months old who are anorectic and chronically ill.<sup>4</sup> Characteristically, pulmonary symptoms are mild, and gastrointestinal manifestations, if present, may not be of sufficient degree to explain the abnormalities.

The etiology of these electrolyte disturbances is multifactorial. During profuse sweating an infant with cystic fibrosis can lose over 80 mEq of Na, 100 of Cl, and 40 of K daily, depending on surface area, state of health, and climatic factors. Not only is there increased sweat electrolyte concentration, but it has been shown that these patients perspire at an abnormally rapid rate, even in the absence of increased ambient or endogenous temperature.<sup>3</sup> The situation is made worse should there be abnormal gastrointestinal losses or inadequate salt intake. In this regard, breast milk and certain types of proprietary milk formulae, whose Na content supplies the 6-8 mEq daily requirements of normal infants, may prove inadequate in the face of excessive sweat losses such as occur in

these patients. This situation if further compounded by the current practices of limiting the amount of salt in commercial baby foods and of delaying introduction of beikost until 4 to 6 months of age.<sup>4</sup> Salt depletion in turn is likely to cause anorexia, further diminishing salt intake. In this connection, though we have no reliable data to permit an estimate of our patient's salt intake before hospitalization, there are reasons to suspect that it was grossly inadequate. Finally, secondary aldosteronism caused by salt depletion increases renal losses of K and H<sup>+</sup>, thus contributing to a state of alkalosis. Unfortunately, serum aldosterone levels could not be done on our patient.

Regarding other clinical manifestations present in our infant, hepatomegaly can occur in CF patients in association with cirrhosis, but this complication usually occurs after several years of illness. Liver biopsy in the present case showed severe steatosis, although at postmortem examination mild fibrotic changes were already in evidence. In view of the patient's deplorable socioeconomic background, poor dietary intake was probably the main cause of her malnutrition, since the pancreatic proteolytic enzymes were found to be normal and the appearance of the stool did not suggest steatorrhea. In all probability, chronic salt depletion, by inducing anorexia, contributed significantly to her failure to thrive, as has been reported in other CF patients.<sup>4</sup> As to the initial findings of opisthotonos and bulging fontanel, we cannot explain them with certainty, but it is worth mentioning that increased intracranial pressure has been described in pancreatic fibrosis, in association with hypovitaminosis A.<sup>5</sup>

In summary, this patient reminds us that hypoelectrolytemia with metabolic alkalosis may be an early manifestation of cystic fibrosis of the pancreas, and that a sweat electrolyte measurement should be considered in the evaluation of any infant presenting with such a derangement.

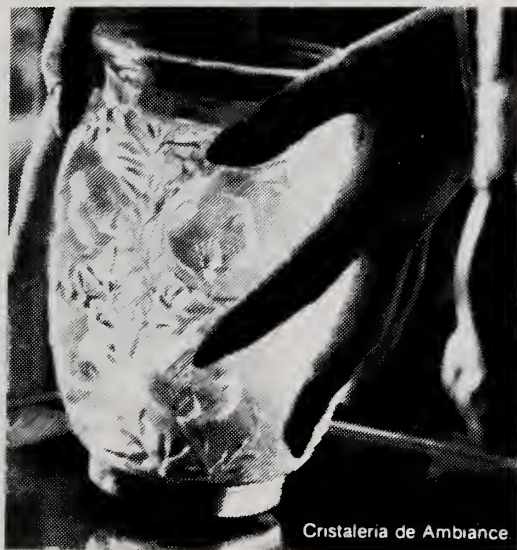
**Resumen:** Se describe un infante de 5 meses de edad con fibrosis quística del páncreas que presentó con depleción de sal, alcalosis metabólica y malnutrición. Se discuten posibles mecanismos implicados en estos hallazgos. Se enfatiza la importancia de considerar la fibrosis quística del páncreas como una posibilidad diagnóstica en infantes que manifiesten los mismos.

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# Sección de Autoevaluación



## ELECTROCARDIOGRAFIA PEDIATRICA

Una niña de 11 años de edad con Artritis Reumatoidea Juvenil (ARJ) en terapia antiinflamatoria con aspirina es referida para evaluación cardiovascular. La niña se queja de dolor retroesternal de dos días de duración que se acentúa con los movimientos inspiratorios. Tiene febrícula de 5 días de duración con picos vespertinos (39°C). Al examen físico se aprecia una niña delgada, con frecuencia cardíaca de 75/min. y extrasístoles ocasionales. No presenta soplos, sonidos de eyección ni frote. Los tonos cardíacos se aprecian disminuidos y los sonidos valvulares son normales.

El hemograma demuestra leucocitosis (18,000) con Hb de 10gm. y Hct. de 30%. La radiografía de torax se reporta con "cardiomegalia discreta" y campos pulmonares normales. El electrocardiograma (ECG) obtenido en esta evaluación inicial se ilustra a continuación:

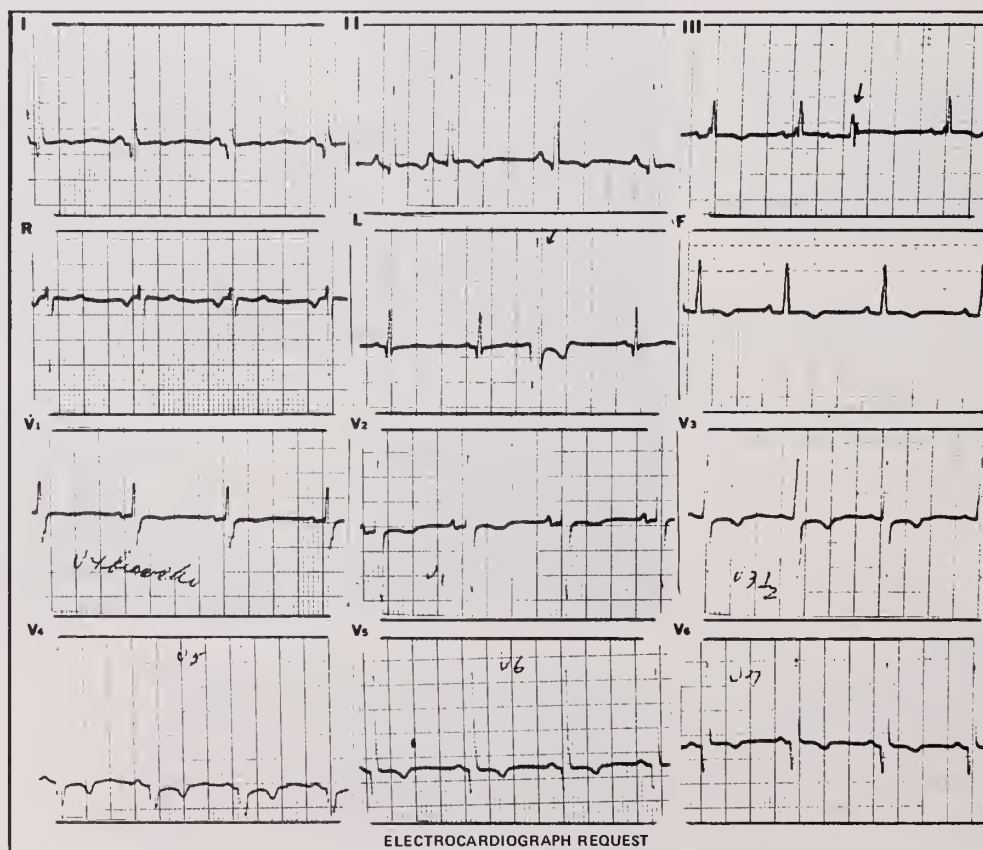


Figura 1. Electrocardiograma inicial al segundo día del dolor retroesternal. Obsérvese la inversión de la onda T en L2,3 y aVF así como en V5-7. Los extrasístoles se señalan con la flecha.

El diagnóstico correcto es:

- a) Fiebre Reumática Activa
- b) Pericarditis
- c) Miocarditis
- d) Fibroelastosis del endocardio
- e) Miocardiopatía hipertrófica obstructiva



## PERICARDITIS

El dolor de pecho en niños no es una manifestación tan frecuente de pericarditis como lo es en el adulto.<sup>1</sup> Cuando ocurre es en la fase inicial de la pericarditis y solo permanece por dos o tres días. Este dolor es causado por envolvimiento de la pleura en proximidad con el pericardio; de ahí que aumente con los movimientos respiratorios.

El frote pericárdico es otro de los hallazgos clínicos prominentes en la pericarditis pero puede estar ausente en ocasiones, como sucede en el caso que discutimos.

La mayoría de los niños con pericarditis desarrollan una *efusión pericárdica* moderada que de por sí no ocasiona síntomas. Cuando esta efusión es severa puede interferir con el llenado diastólico del corazón ocasionando congestión venosa que puede manifestarse con distensión yugular y hepatomegalia. Es frecuente que según la efusión pericárdica aumenta, el frote va desapareciendo, los sonidos cardíacos se hacen más distantes y puede aparecer el *pulso paradójico*. La taquicardia, taquipnea, y la leucocitosis son otros hallazgos presentes en la pericarditis.

La *radiografía de torax* usualmente revela cardiomegalia y a veces los ángulos cardio-frénicos se observan poco definidos, particularmente si hay efusión coexistiendo con el proceso inflamatorio del pericardio.

El *ECG* es muy útil para el diagnóstico de pericarditis aunque algunos pacientes nunca desarrollan cambios electrocardiográficos. Se menciona frecuentemente la disminución en amplitud del complejo QRS en los casos de pericarditis (debido a la efusión pericárdica) pero este no es un hallazgo constante. La presencia de cambios en el segmento ST y la onda T son más consistentes con el diagnóstico de pericarditis. Estos cambios son debido a la afectación del miocardio subyacente, cuyo grado de envolvimiento en el proceso puede ser variable. Si toda la superficie cardíaca está afectada puede manifestarse con elevación del segmento ST en casi todas las derivaciones. Se debe tener siempre en mente que los cambios electrocardiográficos mencionados no son específicos de pericarditis y pueden estar presentes en otras condiciones. Las disritmias y extrasístoles también pueden estar presentes durante la pericarditis.<sup>2</sup>

En la figura 1 se puede apreciar la inversión en la polaridad de la onda T en las derivaciones II, III y aVF así como en las derivaciones precordiales izquierdas. El segmento ST no demuestra alteración significativa pero sí pueden verse extrasístoles nodales (señalados por las flechas) con aberración del segmento QRS.

La *ecocardiografía* ha demostrado ser el procedimiento no-invasivo más efectivo para establecer el diagnóstico de una efusión pericárdica.<sup>3</sup> La presencia de un espacio, usualmente desprovisto de ecos, entre el pericardio y el epicardio confirma la efusión. (Figs. 2 y 3)

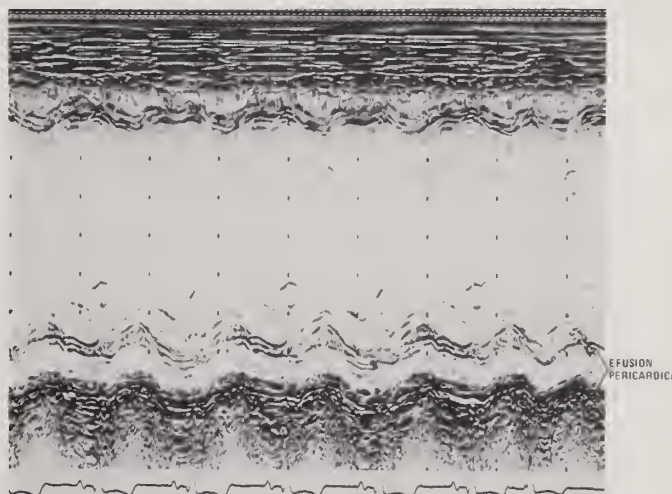


Figura 2. Ecocardiograma modo-M, puede apreciarse la efusión pericárdica.

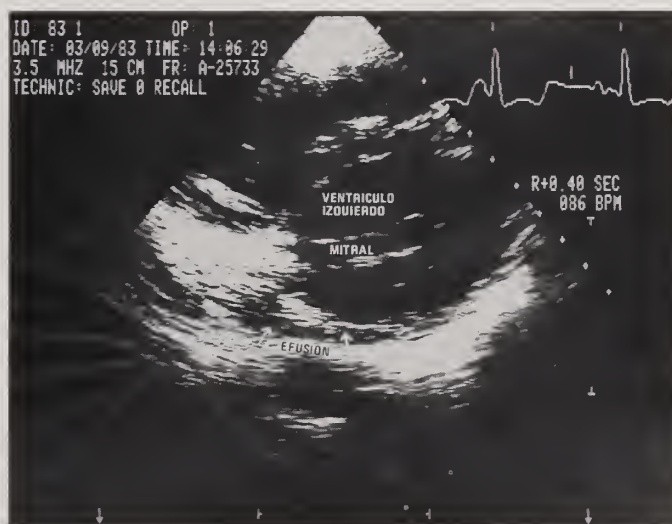


Figura 3. Ecocardiograma bidimensional en plano transverso donde se señala la efusión pericárdica posterior al ventrículo izquierdo.

La incidencia de envolvimiento cardíaco en niños con ARJ es alrededor de 5%, siendo la pericarditis la afectación cardiovascular más frecuente.<sup>4</sup> Es significativo que esta pericarditis aunque está anatómo-patológicamente presente en cerca de 50% de los casos, sólo en 10% de ellos presenta manifestaciones clínicas.<sup>5</sup> La ecocardiografía es capaz de detectar efusiones pericárdicas pequeñas y se ha demostrado evidencia ecocardiográfica de efusión pericárdica en 40% de los pacientes con ARJ.<sup>6</sup>

Aproximadamente 20% de los pacientes con ARJ y pericarditis demuestran cambios en el ECG. Los defectos de conducción, los cambios en la onda P y el segmento QRS son raros. Los cambios en la onda T ocurren con mayor frecuencia que los del segmento ST, y pueden preceder estos últimos. Durante el período de recuperación los cambios electrocardiográficos de ST y T usualmente regresan a la normalidad

(Fig. 4) aunque la dirección de la onda T puede continuar alterada por varias semanas debido a un aumento en la duración del potencial de acción.<sup>7</sup>

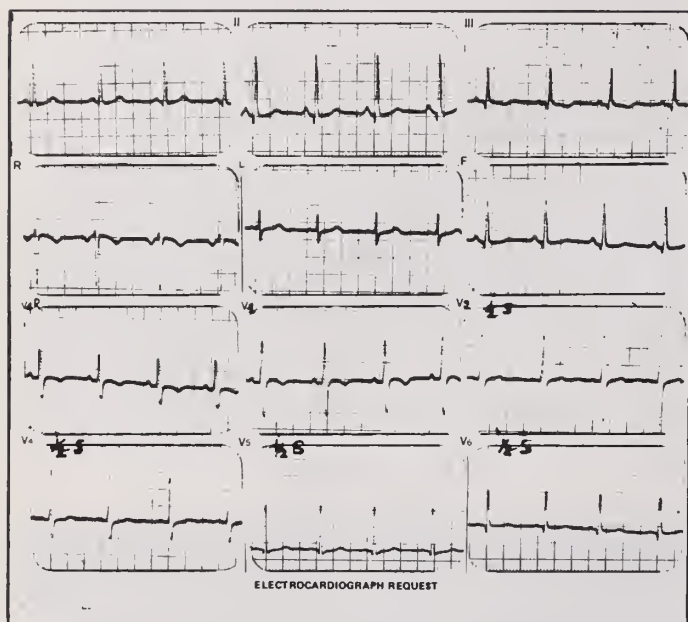


Figura 4. Electrocardiograma normal a las tres semanas del comienzo de la enfermedad y luego de un curso de 10 días de corticoesteroides. Obsérvese la normalización de la onda T y la ausencia de extrasístoles.

En lo que concierne al proceso inflamatorio del pericardio se ha demostrado que estos niños con ARJ se recuperan en un período corto de tiempo sin secuelas cardiovasculares. (Fig. 5 y 6)

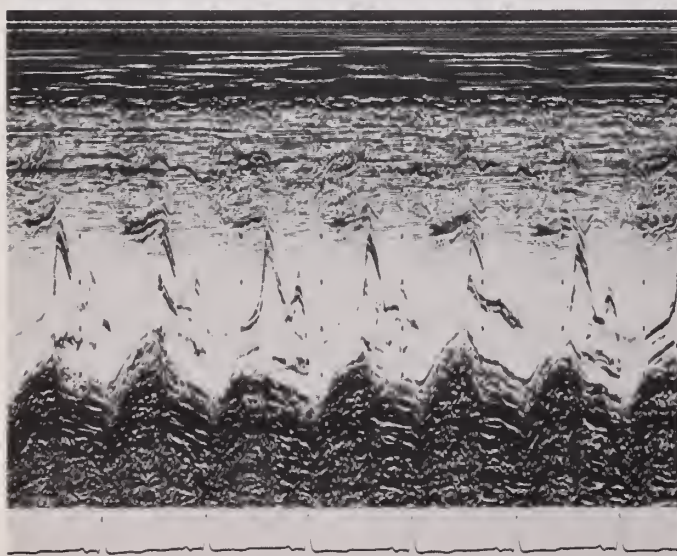


Figura 5. Ecocardiograma modo-M a los 10 días de tratamiento donde ya no se aprecia efusión pericárdica.

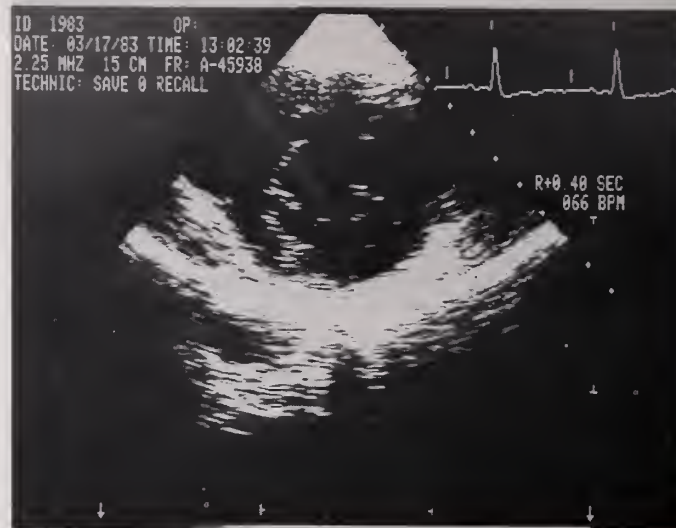


Figura 6. Ecocardiograma bidimensional en plano transversal donde puede observarse la ausencia de efusión pericárdica presente 10 días antes como se demostró en la figura 3.

Por lo regular los pacientes con pericarditis y ARJ no requieren otro tratamiento que el acostumbrado para la artritis reumatoidea. El uso de corticoesteroides está indicado solo en aquellos casos donde no se ha obtenido una respuesta favorable con otros agentes antiinflamatorios o donde coexista una carditis severa.

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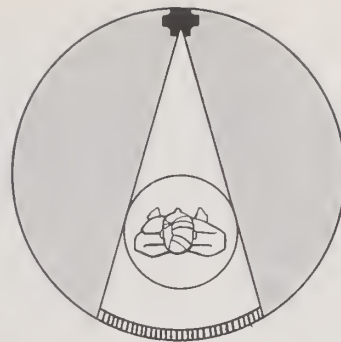


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## Diagnosis



Heriberto Pagán-Sáez, M.D.

An 18 old female born by Cesarean section referred to the Puerto Rico Medical Center because of an enlarged head.

What is your diagnosis?

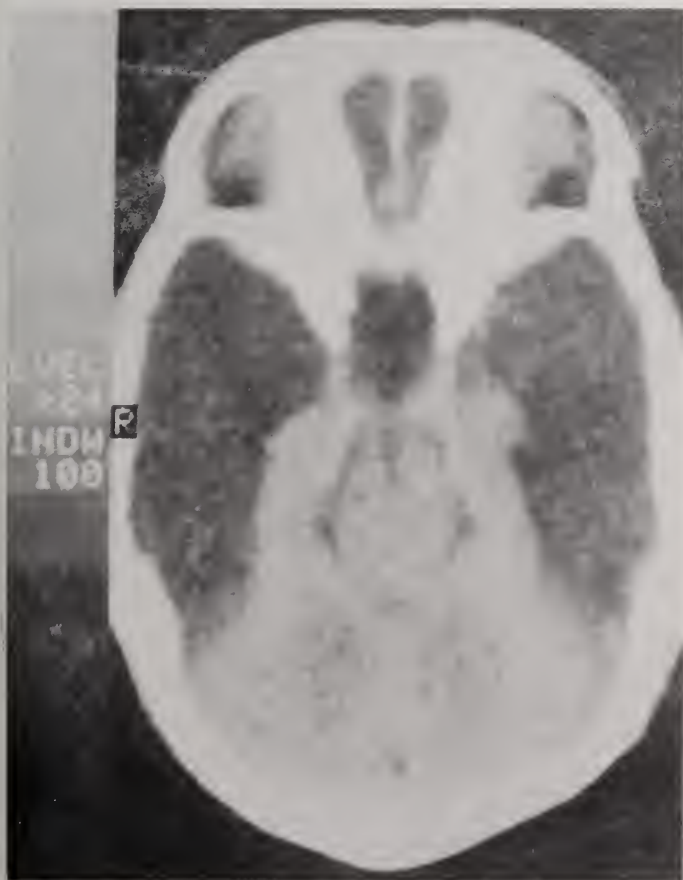


Figure 1.



Figure 2.

*Professor and Chief, Department of Radiological Sciences, School of Medicine, University of Puerto Rico.*

### Diagnosis: Hydranecephaly

Observe the homogenous low density (fluid) occupying the intracranial cavity except for some cerebral tissue along the medial temporal and inferior occipital lobe areas. (Fig. 1)

There is no cerebral mantle identifiable with the mid brain structures seen as a "central island" of tissue (Fig. 2).

Hydranencephaly is said to represent the most severe form of polyporencephaly as the result of encephaloclasia secondary to antenatal bilateral internal carotid artery occlusion.

Reconstruction of the axial images in the mid-sagittal plane (Fig. 3) shows to better advantage the edge of the falx cerebri against the fluid filled supratentorial compartment with residual cerebral tissue in the occipital pole. The brain stem structures are normal.



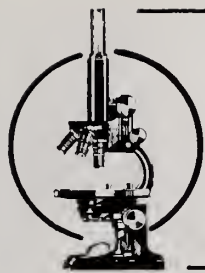
Figure 3.

PRODUCTO MGS. POR SCC COMPONENTES		Acetaminophen Diphenhydramine HCl (Benadryl)	Butabarbital	Carbetapentane	Carbinoxamine	Citric Acid	Codeine	Dextrometorphan	Ephedrine	Guaifenesin	Hydroxyzine HCl	Isoproterenol	KI	Na Citrate	Oxtriphylline	Pheniramine	Phenobarbital	Phenylephrine	Phenylpropanolamine	Phenyltoloxamine	Pseudoephedrine	Theophylline	Tripolidine
Actifed																				30		1.25	
Benylin		12.5																					
Brondecon									100					50									
Co-Tylenol		108					5								.67					10			
Oimetane															2								
Oimetapp															4		5	5					
Oorcol							5		50									6.25					
Fedahist															2					30			
Fedahist Exp.									100						2					30			
Isuprel								4				18	50			2					15		
Marax								5.25		2.5											32.5		
Mudrane GG								4	26							2.5					20		
Naldecon															0.5		1.25	5	2				
Nilcol							5		33						0.7			8					
Novahistine OMX							10		100											30			
Quibron									30												50		
Quibron Plus			8.33						8.33	33											50		
Robitussin										100													
Robitussin OM								15		100													
Rondec					4																60		
Sudafed																					30		
Triaminic															2				12.5				
Triaminic Exp.									100										12.5				
Trind															2				12.5				
Tussar OM								15							2		5						
Tussar 2				7.5		20	10			50				130	2								

Observe que:

- (1) La misma medicina cambia su composición con los años, ej.: Trind.
- (2) Medicinas con prácticamente el mismo nombre, pero composición muy diferente, ej.: Tussar.





# PATHOLOGY *Review*

*Maria Castillo, M.D.*

**J**oven de diez y siete años de edad con dolor a la palpación en el lado derecho de la cabeza.

La radiografía demostró una lesión solitaria, bien circunscrita con destrucción lítica, focal del hueso parietal. (Fig. 1 y 2).

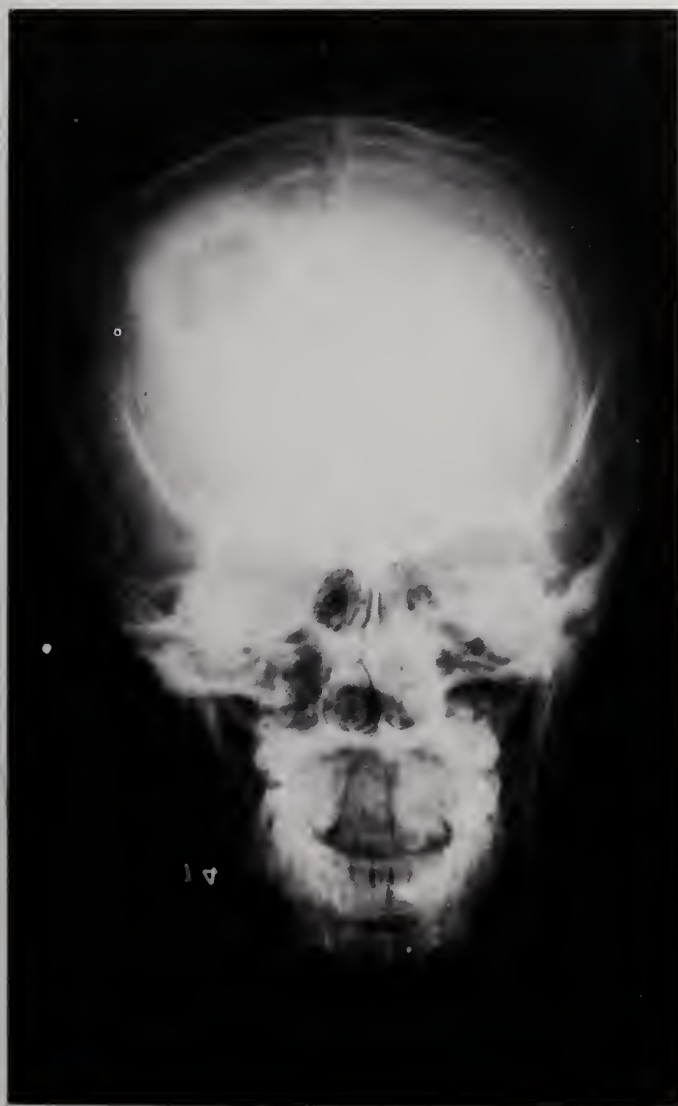


Figura 1. Radiografía de cráneo, proyección anteroposterior.



Figura 2. Radiografía de cráneo, lateral.

¿Cuál es su diagnóstico?

- A. Sarcoma osteogénico
- B. Encondroma
- C. Granuloma eosinofílico
- D. Mieloma múltiple
- E. Condrosarcoma

## Granuloma Eosinofílico

El granuloma eosinofílico comparte con la enfermedad de Letterer-Siwe y la enfermedad de Hand-Schuller Christian una triada de condiciones clínicas raras de etiología desconocida llamadas "Histiocitosis X" las cuales tienen en común una proliferación anormal de los histiocitos, o sea, de los monocitos macrófagos. Clínicamente estas son enfermedades de la niñez y las manifestaciones dependen de los órganos infiltrados que suelen ser huesos, piel, pulmones, hígado, bazo y médula ósea.

Los hallazgos patológicos de las biopsias de estas enfermedades son idénticas y están caracterizadas por un infiltrado difuso de histiocitos, células gigantes, una variable proporción de eosinófilos, células plasmáticas, neutrófilos y linfocitos. Las lesiones tardías presentan histiocitos con citoplasma rico en lípidos, granulomas, células gigantes y fibrosis. (Fig. 3)

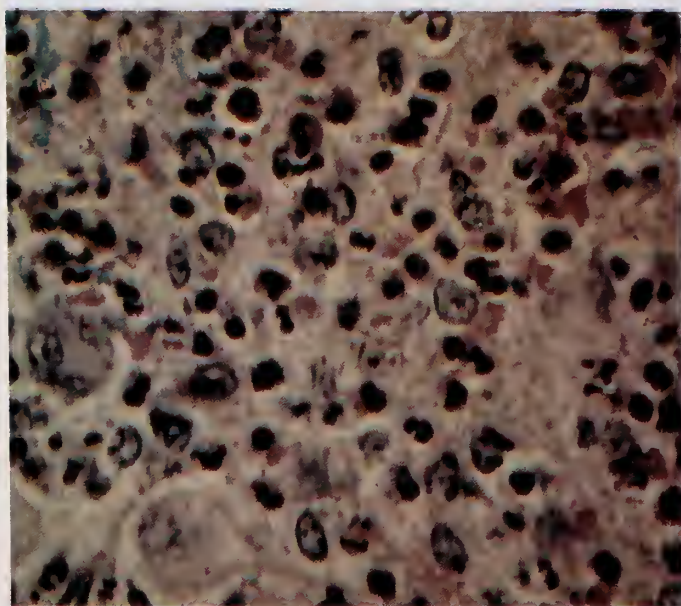


Figura 3. Detalle histopatológico del granuloma eosinofílico.

Las histiocitosis están siendo consideradas enfermedades de origen inmunológico, pues la mayoría de los pacientes presentan deficiencia de los linfocitos T supresores y algunos responden a extracto tímico y quimioterapia. La enfermedad de Letterer-Siwe es la forma diseminada aguda que ocurre en infantes menores de 18 meses y es la variante de peor pronóstico. Usualmente varios órganos o sistemas están envueltos. La enfermedad de Hand-Schuller-Christian ocurre en niños entre las edades de dos a tres años. Los pacientes presentan lesiones óseas múltiples, diabetes insípida y exoftalmo.

El granuloma eosinofílico ocurre en niños mayores entre las edades de cuatro a siete años y en adultos. Se presenta como una lesión ósea, solitaria o a veces múltiple sin manifestaciones viscerales y es la variante clínica de mejor pronóstico.

El tratamiento es curetaje quirúrgico de la lesión o radioterapia.

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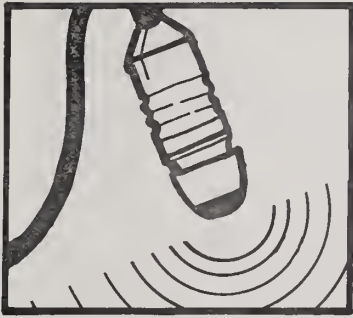
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# Sonography Quiz

Rafael M. Rivera, M.D.

The patient was a 3 years old girl who presented with vaginal bleeding. Fig. A. is a transverse sonographic section through the lower aspect of the pelvis. Fig. B is a lateral radiographic view of a simultaneous cystogram and barium enema.



Figure A



Figure B

The most likely diagnosis is:

- A. Precocious puberty
- B. Hematometra
- C. Sarcoma Botryoides
- D. Ovarian cyst

## CORRECT DIAGNOSIS: C. Sarcoma Botryoides



Figure C

**Discussion:**

The low pelvic sonographic transverse section (fig. A) showed a solid, polypoid mass posterior to the bladder in the anatomic location of the uterus and upper vagina. The simultaneous cystogram and barium enema (fig. B) demonstrates a wide separation between the bladder and the rectum outlining the size of the tumor. The rectum and bladder were uninvolved. Fig. C is the lateral view of a vaginogram showing the large polypoid mass manifested as multiple filling defects in the upper aspect of the vagina. In true precocious puberty there are no abnormal pelvic masses. The findings are a small but stimulated uterus presenting the fundus larger than the cervix as seen in post-pubertal patients. Hematometra and hemotocolpos present sonographically as well demarcated tubular cystic structures confined to the anatomic cavities of

the uterus and vagina and not as solid polypoid masses. Ovarian cysts are adnexal lesions and are easily differentiated from the uterus by their lateral position. Although predominantly cystic the rare dermoid cysts may have solid contents.

Rhabdomyosarcoma is the most common soft tissue sarcoma in the pediatric age and accounts for 10% of all cancers seen in childhood. Sarcoma botryoides represents the embryonal type of rhabdomyosarcoma. The descriptive term is applied to a polypoid, grape-like malignant neoplasm arising from the lower end of the embryonic Mullerian tubercule. Sarcoma botryoides of the vagina usually manifests itself during the first four years of life and occasionally is present at birth. Clinically, the tumor presents as a polypoid vaginal mass associated with vaginal bleeding. Clusters of tumoral masses may be extruded or may present themselves at the introitus. The sonographic findings are a solid, inhomogeneous mass located behind the bladder in the mid aspect of the lower pelvis. The urinary bladder may be involved by the tumor in advanced cases. The echographic characteristics of the lesion may resemble that produced by hydatiform moles. This similarity is due to the grape-like gross pathology of both tumors.

Sarcoma botryoides is an almost invariably fatal condition even if treated with radical surgery, chemo or radiotherapy. On the occurrence of vaginal bleeding in any young child the possibility of this serious neoplasm must not be overlooked.

**Suggested Reading**

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# Resúmenes de La Literatura Médica



**TAQUICARDIA SUPRAVENTRICULAR EN INFANTES: USO DEL REFLEJO DE INMERSION.** Sperandeo V., Pieri D. Palazzolo P., et al. *Am J. Cardiol* 51:286, 1983.

La taquicardia supraventricular (TSV) es una emergencia pediátrica frecuente en infantes y es mandatoria su conversión al ritmo sinusal. Las maniobras vagales (masajes carotídeos, inducción de vómito, etc.) pocas veces logran terminar el episodio de TSV. Con la inmersión súbita en agua puede lograrse la terminación del episodio aunque este procedimiento no se ha utilizado con frecuencia en infantes.

Los autores reportan su experiencia en el Hospital Pediátrico de Palermo en Italia utilizando esta maniobra para terminar los episodios de TSV en infantes. Informan de 10 infantes menores de 6 meses de edad con TSV y a quienes luego de ciertas precauciones para evitar la aspiración, se les sumergió la cara en agua a temperaturas de 5 a 6°C por espacio de 6 a 7 segundos. En todos los casos hubo conversión inmediata a ritmo sinusal. No se reportan complicaciones durante e inmediatamente después de la maniobra, incluso en aquellos que tomaban digoxin.

El reflejo de inmersión consiste de bradicardia y vasoconstricción periférica que tiene como resultado un aumento en el flujo sanguíneo al cerebro y al corazón. La estimulación de los terminales aferentes de los nervios de la cara por el agua fría inicia el reflejo. Por la facilidad de aplicación, su alto índice de efectividad y la ausencia de complicaciones es que los autores recomiendan esta maniobra como el primer paso terapéutico en infantes con TSV persistente.

Rafael Villavicencio, M.D.

**ENVOLVIMIENTO DE LOS RIÑONES POR LEUCEMIA EN NIÑOS: HALLAZGOS EN TOMOGRAFIA COMPUTARIZADA.** Tsutomu Araki: *Journal of Computer Assisted Tomography* 6: 781-784 (University of Tokyo Hospital, 7-3-1, Hongo, Bunkyo-ku, Tokyo, Japan).

A pesar de que el envolvimiento leucémico de los riñones en niños es aparente en las autopsias de un 50% de estos pacientes, la documentación clínica o radiológica de este es

raras veces encontrada. Este artículo nos describe a 5 pacientes con envolvimiento renal por leucemia demostrado por tomografía computarizada. Los hallazgos incluían agrandamiento difuso bilateral de los riñones (2 casos), agrandamiento difuso unilateral renal (1 caso), masa intrarenal bien definida (1 caso) y masa en la región hilar del riñón (1 caso). Tres de estos que recibieron radioterapia local respondieron bien a este tratamiento en relación a sus hallazgos renales. Los autores concluyen que la tomografía computarizada tiene valor en el diagnóstico de envolvimiento renal por leucemia, en la planificación de radioterapia, y en la evaluación de los resultados del tratamiento.

Bernardo Marqués, M.D.

**ACUTE SINUSITIS IN CHILDREN.** Wald E. R. *Pediatric Infectious Disease* 2: 61-68, 1983.

En la mayoría de los niños que sufren de sinusitis los senos maxilares están afectados, al igual que los etmoidales. Después de los 10 años de edad los frontales adquieren mayor importancia clínica. La sinusitis esfenoidal por lo general sucede cuando hay pansinusitis. Los síntomas más comunes de la sinusitis en los adultos y adolescentes son dolor facial, cefalea y fiebre. En los niños las manifestaciones son menos características. Puede que sean las de un catarro de mayor severidad y con más fiebre que lo esperado; rinorrea purulenta abundante; edema periorbital; con menos frecuencia cefalea o dolor referido a la dentadura. Un catarro que persiste por más de 10 días asociado con tos y rinorrea sugiere la posibilidad de sinusitis. Los signos más importantes son la rinorrea purulenta, dolor a la palpación de la cara, el edema periorbital y fotorris. Ayudan a confirmar el diagnóstico la transiluminación, las radiografías y la ultrasonografía. Los hallazgos radiográficos comprenden niveles de líquido y engrosamiento de las mucosas de más de 4mm. Los cultivos de las secreciones nasales no reflejan el verdadero agente etiológico; éste se identifica solamente por medio de la punción y aspiración del seno, pero en la mayoría de los casos este procedimiento no está indicado. Los agentes etiológicos más comunes son *Streptococcus pneumoniae*, (*neumococo*), *Branhamella catarrhalis* (Neisseria) y *Haemophilus influenzae*. El tratamiento de elección consiste en ampicilina o amoxicilina. En los casos de resistencia a



éstos o alergia a la penicilina se pueden emplear cefaclor, trimetoprim-sulfametoxazol o eritromicina con sulfisoxazol. El tratamiento debe prolongarse por 10 a 14 días. La eficacia de los antihistamínicos y descongestivos no se ha establecido en estos casos. Las complicaciones principales se deben a la extensión de la infección a la órbita, huesos y estructuras intracraneales.

Jose E. Sifontes, M.D.

#### **HIGH FREQUENCY VENTILATION FOR IMMATURE INFANTS. Special Conference Report. Pediatrics 71: 280-287, 1983.**

La ventilación mecánica de los neonatos inmaduros está asociada con un aumento de las complicaciones pulmonares algunas de las cuales pueden ser incapacitantes o letales. Se han postulado como los factores precipitantes barotrauma, oxigenotoxicidad, trastornos circulatorios, sobrecarga de líquidos y otros. Estos problemas han despertado gran interés en la ventilación con altas frecuencias como método de evitar los mismos. La ventilación con altas frecuencias respiratorias de 60 a 2400 por minuto (1 a 40 Hz). Existen varios métodos de administrarla: a chorro, oscilatorio y variaciones de estos. En animales experimentales y en algunos neonatos permite la oxigenación adecuada y la eliminación de CO<sub>2</sub>. Los mecanismos no están bien establecidos; es probable que el intercambio de gases se lleve a cabo a lo largo de todo el tracto respiratorio. Aunque a corto plazo la ventilación con altas frecuencias parece ser bien tolerada no se saben los efectos adversos a largo plazo y menos aún los que podrían suceder con los diversos aparatos que se están ensayando. Se concluye que son necesarios estudios clínicos bien planeados y fiscalizados que permitan obtener la información precisa y que pueda ser utilizada lo mas rápidamente posible para disminuir la morbilidad y mortalidad de la ventilación mecánica del neonato.

José E. Sifontes, M.D.

#### **ESOPHAGEAL AND GASTRIC ABNORMALITIES IN GASTROESOPHAGEAL REFLUX DURING INFANCY. AC Hillemeir, BB Grill, R. McCallum and J. Gryboski. Gastroenterology 84: 741-6, 1983.**

Los autores evaluaron 34 infantes con síntomas de reflujo gastroesofágico por medio de manometría esofágica, prueba de reflujo ácido y estudios de vaciamiento gástrico. Los infantes con pobre crecimiento y/o enfermedad pulmonar recurrente tuvieron reflujo más severo por pH esofágico que pacientes sin complicaciones serias por su reflujo. Las presiones del esfínter esofágico inferior no tuvieron variación entre los grupos con enfermedad leve o severa. Más importante, infantes con enfermedad seria secundaria al reflujo demostraron una disminución en la amplitud de peristalsis esofágica distal y un vaciamiento gástrico lento de fórmula a base de leche de vaca marcada con isótopo. Los resultados proveen más evidencia a favor de un desorden

general de motilidad del tracto gastrointestinal superior en infantes con reflujo gastroesofágico severo.

**Comentarios:** Los pediatras, con demasiada frecuencia, visualizan el reflujo gastroesofágico (RGE) en infantes como un pobre funcionamiento del esfínter esofágico inferior (EEI) exclusivamente. Luego es frustrante cuando el manejo tradicional encaminado a poner una "distancia" entre el contenido gástrico y el EEI, no da resultados consistentes. De igual manera, el efecto impredecible de betanecol, una droga que aumenta la presión en descanso del EEI. La literatura reciente está estableciendo claramente que el RGE en infantes representa un disturbio de motilidad generalizada del tracto gastrointestinal alto.

Un primer paso en esta dirección fue dado por el grupo de Jolley (Am J Surg. 138:946, 1979) cuando pudieron identificar en infantes con RGE dos patrones de reflujo basados en pruebas de pH esofágico.

Un primer patrón lo exhibían aquellos infantes con hernia de hiato y un por ciento grande ellos requirió cirugía. Un segundo patrón, sin embargo, se vió en pacientes con síntomas pulmonares, diarreas recurrentes y antropiloroespasmo por radiografías. Muy pocos de estos infantes fueron sometidos a cirugía. En este último grupo, el RGE probablemente se debe a un pobre vaciamiento gástrico secundario al antropiloroespasmo. Vemos esta sintomatología frecuentemente en intolerancias a las leches y la designamos "gastropatía alérgica". La terapia posicional, alimentos sólidos y el betanecol no son de gran ayuda en estos pacientes. Vemos, entonces, como en infantes con RGE, el trazado de la prueba de reflujo ácido (pH esofágico) puede anticiparnos la patofisiología envuelta y sugerir el manejo.

El estudio de Hillemeir et al, corrobora que en muchos infantes que exhiben consecuencias serias de RGE, el factor determinante no es un EEI débil, sino un vaciamiento gástrico pobre y una peristalsis disfuncional del esófago distal. El apreciar el desorden difuso de motilidad gastrointestinal que existe en RGE de la infancia nos permitiría decidir la posible efectividad de nuevas terapias. La metoclopramida, por ejemplo, que aumenta la velocidad del vaciamiento gástrico, ya se está evaluando en infantes con RGE (Am J Dis Child 136: 299, 1982) y promete ser una droga útil.

E. Cichowicz-Emmanuelli, M.D.

#### **THE ENDORECTAL PULL-THROUGH FOR THE MANAGEMENT OF ULCERATIVE COLITIS IN CHILDREN AND ADULTS: Coran, A.G., Sarahan, T.M., Dent, T.L. et al Annals of Surgery 197: 99, 1983.**

The authors report on an approach being recommended with increasing frequency from several surgical centers. The use of an endorectal pull through of ileum following total colectomy for ulcerative colitis offers the advantages of anal continence without the need of a permanent ileostomy. Twenty six children and adults with ulcerative colitis underwent this procedure with remarkably good results. There were few complications in the postoperative period. All patients acquired day and night continence. However, they reported a high frequency of bowel movements, averaging seven per day, and ranging from two to twenty. Most

patients were satisfied with the advantages offered by this procedure. However, two patients requested reconversion to an ileostomy because of an unacceptably high frequency of stools.

It appears that this is a worthwhile alternative to patients with ulcerative colitis that require total colectomy. The technical difficulties of the procedure might be minimized using a recently reported method of chemical debridement of the rectosigmoid mucosa, instead of the tedious surgical dissection needed to create the endorectal pouch. Longterm results with this new technique must be analyzed in the future.

Pedro J. Roselló, M.D., F.A.C.S., F.A.A.P.

#### SIGNIFICADO CLINICO DE LA RESISTENCIA A CLINDAMICINA POR BACTEROIDES FRAGILIS:

Yee, Marcia, H., et al: JAMA 248: 1860-1863, 1982.

El grupo de bacterias *Bacteroides fragilis* son las más numerosas en el colon y las bacterias anaeróbicas que se recobran más comúnmente en infecciones en los humanos. A pesar de que el hidrocloreuro de clindamicina se considera aún como el antibiótico de elección en el tratamiento de infecciones causadas por estas bacterias, se están encontrando cepas resistentes. Este grupo repasa 14 expedientes clínicos de pacientes infectados con cepas de *B. fragilis* resistentes. El tener cepas resistentes jugó un papel importante en 4/14 pacientes. Tres de 4 recobraron solo al utilizar antibióticos efectivos. Siete pacientes habían recibido eritromicina o clindamicina antes de recobrar las cepas resistentes.

El estudio nos señala que en el caso de un paciente que tenga una infección causada por *B. fragilis*, debemos saber si es posible, la susceptibilidad a clindamicina; de lo contrario asúmase que es resistente y utilice un antibiótico apropiado.

**Nota:** Para cepas de *B. fragilis* resistentes debe considerarse metrodinazole endovenoso. Sospeche cepas resistentes en pacientes que no responden a tratamiento, especialmente aquellos que estuvieron recibiendo eritromicina o clindamicina. Esté seguro de que no exista una acumulación de pus.

Carlos H. Ramírez-Ronda, M.D.

#### SUCCESSFUL TREATMENT OF HBs AND HBeAg POSITIVE CHRONIC LIVER DISEASE: PROLONGED INHIBITION OF VIRAL REPLICATION BY HIGHLY SOLUBLE ARABINOSIDE 5' - MONOPHOSPHATE (ARA-AMP)\*. Weller IVD, Bassendine MF, Crapi A, et al. Gut 23: 717-723, 1982.

ARA-A (adenine arabinoside) tiene efecto anti-viral contra virus que contienen DNA y se ha utilizado previamente para tratar pacientes con hepatitis crónica debido a hepatitis viral tipo B. ARA-AMP es derivado de ARA-A, es más soluble en agua y tiene la ventaja que se puede administrar intramuscularmente. Los autores le administraron ARA-AMP a ocho pacientes con hepatitis crónica activa debida a infección con hepatitis viral tipo B. A cinco pacientes se les

administró en dosis de 10 a 15mg/kg/día por diez días y hubo evidencia de inhibición de replicación viral durante la terapia. Los marcadores virales séricos aumentaron una vez terminada la terapia. A los otros tres pacientes se les dio una terapia de ARA-AMP más prolongada (de 21 a 39 días) utilizando una dosis menor (5mg/kg/día). En éstos hubo disminución de los marcadores virales durante la terapia seguido por una elevación por tiempo variable al terminar la terapia y finalmente una desaparición de los marcadores y desarrollo de anticuerpos contra el antígeno e. Los autores comentan que esta terapia puede ser beneficiosa porque disminuye la cantidad de virus y permite a las defensas del individuo eliminar el virus residual. Estudios controlados se deben llevar a cabo para confirmar estos hallazgos.

Angel Olazabal, M.D.

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## AMERICAN ACADEMY OF PEDIATRICS

### PEDIATRICIANS PROPOSE MEDICAID STANDARDS FOR CHILDREN

A Medicaid policy statement, setting out minimum benefits and eligibility standards for poor children cared for under the government health program, has been sent to public health policy makers and key congressional leaders by the American Academy of Pediatrics.

Said R. Don Blim, M.D., FAAP, chairman of the Academy's Committee on Child Health Financing which developed the statement, "The major gains made in the last decade by poor children under Medicaid are being threatened by recent federal policies and state fiscal crises. Changes in eligibility criteria and limits on mandatory and optional services are disproportionately affecting children, the largest population group covered by Medicaid".

To minimize the effects on children of recent tightening of Medicaid benefits, the AAP recommends that restrictive eligibility criteria be expanded; that a comprehensive list of services be covered; that arbitrary limits on the amount, duration and scope of services be eliminated; that administrative efficiency be improved to contain costs; and that office-based physicians be reimbursed at fee levels to ensure their participation in Medicaid.

Regarding eligibility, the policy says:

- categorical limits, such as covering only children from single-parent families, should be eliminated;
- a uniform income standard must be maintained, allowing for some regional cost-of-living variations; and
- unborn and newborn children in eligible families should be automatically defined as eligible.

The minimum benefits for children includes services for health supervision, acute care and chronic as well as catastrophic disease. The statement says some of the program's services which states do not have to provide now, such as prescriptions and dental care, should be required nationwide. It also says medical services provided for children under Medicaid's Early and Periodic Screening, Diagnosis and Treatment Program (EPSDT) should be provided by a physician who gives continuing care, using the AAP's recommended schedule for perio-

dic health supervision visits.

If Medicaid should be taken over from the states by the federal government, says the AAP policy, states now offering more comprehensive benefits than a federal minimum should be required to maintain those benefits, with the federal government continuing to share the expenses.

Based on AAP research showing that low reimbursement rates cause physicians to leave the Medicaid program, the policy says doctors must be paid adequately to ensure that children receive continuing care. The Academy policy supports testing of different ways to reduce costs, adding that cost containment "must not impair the quality of care," but specifically rejects the idea of copayments being charged for preventive care and health supervision.

The AAP's Blim said newborns requiring intensive care, chronically ill children and adolescents are among the poor who already have inadequate Medicaid coverage and whose care is most likely to suffer from Medicaid restrictions.

The AAP said it reviewed Medicaid policy research for more than a year and, during the study, also developed a background paper, "Medicaid and Children: A Policy Analysis". The policy statement and background paper are available by writing to: Department of Child Health Finance and Organization, AAP, P.O. Box 1034, Evanston, IL 60204.

### PEDIATRICIANS OPPOSE FEDERAL RULE ON HANDICAPPED NEWBORNS

The American Academy of Pediatrics and the National Association of Children's Hospitals and Related Institutions announced that they filed suit in federal court in the District of Columbia against the Department of Health and Human Services' rule on disclosure of treatment of severely handicapped newborns and intervention by federal authorities.

AAP called the "Baby Doe" rule "a dangerous and unprecedented intrusion into the nation's pediatrics wards."

AAP President James S. Strain, M.D., said the rule, which requires hospitals to post hotline numbers in their wards and encourages people to report suspected cases of withholding food or medical treatment from handicapped newborns, "could actually harm an infant or cause its death."

Strain said the Academy and other medical and health related organizations have written to HHS Secretary Margaret Heckler objecting to the haste with which the rule is being implemented—only 15 days after the rule was issued rather than allowing the normal 60 days for public comment. Strain expressed a desire to work with HHS to protect children who can benefit from necessary and appropriate medical treatment. But, he said, the Secretary should realize that the government's procedure, scheduled to go into effect soon are "dangerously negative" and "hasty, arbitrary and simplistic".

HHS procedure call for hospitals which receive federal assistance to post notices in pediatric and maternity wards and intensive care nurseries warning that failure to feed and care for handicapped infants is prohibited by law and that anyone who believes an infant is being denied food or "customary medical care" should call an HHS hotline or the state's child protective agency.



Since there are no established criteria for customary medical care, the AAP said federal and state civil rights investigators or social workers sent to look into complaints will be unable to determine what treatments are appropriate.

As an alternative to the HHS rule, Strain said the Academy proposes that hospitals establish review procedures for handicapped infants and local panels, composed of medical ethics committees and others, on a trial basis, to review the procedures.

The AAP's president pointed out the difficulty of deciding when it is appropriate to attempt extraordinary treatments for inevitably fatal conditions. For example, non-medically trained investigators could not be expected to know about the controversy over whether closure of a spinal defect in an infant with hydrocephalus should sometimes be delayed until the hydrocephalus has been relieved. Strain noted that there are legitimately differing views of appropriate treatment in many cases.

### PEDIATRICIANS TESTIFY AGAINST 'BABY DOE' LEGISLATION

The American Academy of Pediatrics testified in a Senate subcommittee hearing in support of local hospital review of difficult medical decisions involving life-sustaining treatment of severely ill newborns.

The Academy also said the recently imposed Health and Human Services Department rule which established hospital "hotlines" to a Washington office for reporting complaints about treatment of such infants will not save babies' lives. An AAP representative said it will only "worsen prospects for progress" in dealing with the medical dilemmas.

George A. Little, M.D., chairman of the Academy's Committee on Fetus and Newborn, told the Subcommittee on Family and Human Services, chaired by Sen. Jeremiah Denton (R-Ala.), the AAP also opposes any legislation that would try to prescribe medical treatment for severely ill infants.

The HHS regulation took effect March 22 and requires hospitals which receive federal funds to post hotline numbers in pediatric, maternity and intensive care units on signs encouraging anyone who thinks that an infant is being denied food or receiving improper treatment to call HHS. The AAP had sought to delay the effective date of the rule to permit more study.

In this testimony, Little said the Academy supports the recommendation of the President's Commission on Bioethics that decisions about life-sustaining treatment should be made by local review bodies. These could be composed of physicians, parents, other laymen, nurses, social workers, and ethicists.

Little, a neonatologist and chairman of the Department of Maternal and Child Health at Dartmouth Medical School (Hanover, N.H.), said that while such boards exist in many hospitals, guidelines are needed for their use and urged that these review bodies be established everywhere.

The neonatologist said the AAP supports the intent of the so-called "Baby Doe" rule but that HHS misconstrues the issue as one of discrimination, whereas it is really the definition of what care is appropriate in individual cases.

The most difficult cases, he said, are those in which medical

science does not know whether treatment will benefit the baby. He said the Academy and the presidential commission agree that for the many infants born prematurely, and sometimes those with serious birth defects, all that is certain is that without intensive care they are unlikely to survive.

Little said physicians differ on the best course of action in some cases and, while this is true in medicine for any age group, it is especially so in the developing specialty of neonatology. HHS' "intrusive procedure", he said, has not been used in any other area of medicine. He said it could force a physician to change a course of treatment or provide medical care simply out of fear of the federal government.

Little further noted the HHS rule could prolong futile life support indefinitely with pain and suffering to the child, and "misuse of scarce and vital medical resources with enormous expense to the community".

He pointed out that the HHS rule does not address the issue of confidentiality of medical records and discussions between physicians and parents. He added that responding to inquiries from federal investigators could breach such traditional trust relationships.

Relying on local child protective agencies for investigations, where their staffs have no experience with procedures involving newborns with handicaps, will only reduce the effectiveness of these financially stretched agencies in doing the work for which they were created, the AAP maintained.

The Academy called the HHS remedy "untimely, cumbersome and untried", adding that in situations where death is inevitable, "It well may lead to overtreatment of many infants with every technology available... against the best interest of the infants, simply prolonging the process of dying." The AAP accused HHS of trying to correct a situation it has not even identified.



### AMERICAN MEDICAL ASSOCIATION

The American Medical Association is sponsoring a National Conference entitled: **Impact of Lifestyle on Child and Adolescent Health: Prevention and Treatment**. The meeting will be held September 8-10, 1983 at the Hyatt Regency Chicago. The purposes of the conference are: 1) to focus attention of physicians and community leaders and organizations on the serious developmental and health problems faced by children and adolescents and 2) to focus attention on the great and often unrealized potential that physicians have to assist individuals and communities in the prevention and treatment of problems of development and lifestyle.

Recent national and state reports have documented the basic child and adolescent problems. Accidents and injuries now account for half of the deaths of children and youths ages 1-17. In 1979, 72% of had drunk alcohol, 34% had smoked a cigarette and 37% had smoked marijuana. There are over one million abused children per year in the USA. Suicide and homicide are two of the leading causes of death among teenage males, and are a growing phenomena among teenage females. One-third of all sexually active teenagers become

pregnant/year and have a high incidence of premature births. Information now exists that atherosclerotic heart disease may have antecedents in childhood dietary habits.

These are problems related to lifestyles. They create specific health problems for treatment by the physician and have a serious impact on the total cost of health care and on the facilities that must be provided. These problems also create a tremendous loss of productive life.

What physicians and communities need is a joint opportunity not only to learn about the magnitude and manifestations of these problems, but also to become motivated and informed about possible approaches to effective prevention and treatment. This conference will highlight the problems and some effective applicable programs and ideas from experts.

Registration fees are: AMA physicians \$75.00, non-member physicians \$150.00, non-physicians \$75.00, AMA member med students and residents Free, non-member medical students and resident \$35.00.

Conference brochures containing registration and room reservation forms will be available May 1, 1983. Please contact Eltha Thomas —(312/751-6376) or Desiree Goodwin — (312/751-6445). Both of the above contacts are at the AMA office, 535 North Dearborn Street, Chicago, Il. 60610. Please address all inquiries to them.



**AMERICAN ASSOCIATION  
OF BLOOD BANKS**

**AABB PEDIATRIC HEMOTHERAPY  
COMMITTEE CREATED**

A newly established committee has been formed to foster the knowledge and understanding of blood transfusion therapy in the neonate and the pediatric patient. The Pediatric Hemotherapy Committee is a full committee within the structure of the AABB. The genesis for this committee has been almost universal concern that hemotherapy for the pediatric patient, and for the neonate in particular, needs to be less random and have more structured guidelines. In addition, accessible reference resources need to be established.

1. With the Workshop committee, it has developed a workshop for the 1983 AABB Annual Meeting which will give a general educational outline of hemotherapy in the neonate and cover many of the problems and indications related to administration of blood components in the neonatal patient.
2. A research and progress (RAP) session will be presented at the Annual Meeting to discuss cytomegalovirus and the appropriate transfusion therapy of the newborn. Other controversial areas will be considered for the future.
3. The Committee encourages the submission of scientific and administrative abstracts specifically covering all aspects of pediatric and neonatal transfusion research and practice.
4. The Committee plans to establish a liaison with the American Academy of Pediatrics, to centralize and

encourage research relating to hemotherapy of the pediatric and neonatal patient.

5. Interaction will be encouraged among those concerned with administrative, technical and medical aspects of hemotherapy of the newborn in particular and the pediatric patient and advise other AABBB committees.

The committee was established at the post-Anaheim board meeting and as can be seen, several of the Committee's charges have already been addressed with added emphasis on pediatric hemotherapy given at the Annual Meeting. A call for abstracts has been published in the pediatric literature and accepted abstracts will be brought together in a separate session on pediatric hemotherapy research and practice.

For more information on the purpose and function of this committee, questions may be addressed to the co-chairmen, Laurence Sherman, M.D., Director, American Red Cross Blood Services, St. Louis, MO, (314) 658-2103, and Ronald Sacher, M.D., Georgetown University Medical Center, Washington DC, (202) 625-2660.



**PHARMACEUTICAL  
MANUFACTURERS  
ASSOCIATION**

**PHYSICIAN GROUP CALLS OFF  
ASPIRIN/REYE LAWSUIT**

The Committee on the Care of Children (CCC) filed papers dropping a suit in which the committee had sought a temporary restraining order against a Department of Health and Human Services "public education campaign" on Reye Syndrome.

The CCC announced its decision to withdraw its court action at a press conference "The lawsuit is no longer needed," Dr. Heinz Eichenwald, CCC chairman, said. "The original purposes ... have been accomplished. New studies are being put together. The aggressive publicity campaign ... has stopped. And we believe no warning labels will be required unless the new studies show they are indicated."

Later the same day, HHS Secretary Margaret Heckler issued a statement saying HHS "has made absolutely no change in its policy concerning warnings about the potential link between aspirin and Reye Syndrome ... The HHS public education campaign has not been stopped. It will continue, as planned, through the end of this flu season."

At the CCC briefing, attorney Neil Chayet told of a meeting between committee members, Secretary Heckler, and Assistant Secretary for Health Edward M. Brandt Jr., M.D. The government had assured them, he said, that "no new publicity was being planned." It was subsequent to this meeting that the committee decided to cancel litigation.

The lawsuit, filed in US District Court in Boston last November, sought to halt the HHS publicity which warned physicians and parents against a possible connection between



salicylates and Reye Syndrome, an infrequent but serious complication of flu and chicken pox. The campaign, which includes massive mailings and radio and TV spots, warns against use of aspirin for these conditions in children under age 16.

The CCC, whose members are primarily pediatricians, and other professional groups have declared studies linking aspirin with Reye "seriously flawed," and have urged that new research be conducted under improved protocols.

At the briefing, CCC members said they were pleased that the Institute of Medicine had been chosen to oversee new studies, and that its selection had been a "very significant event" in their decision to drop litigation.

Heckler spoke of the studies in her statement, saying, "we ... believe it is important to resolve as quickly as possible the scientific dispute as to a possible link between aspirin use and Reye Syndrome ... The studies HHS called for will proceed as planned ... Hopefully, these studies will shed light on whether an aspirin warning label is called for."

The Committee on the Care of Children, having halted its Reye/aspirin litigation against the Department of Health and

Human Services will petition HHS to establish guidelines and criteria for judging when public warnings on drug use are necessary.

"It may be a surprise to many, but no such criteria really exist," Dr. Heinz Eichenwald, CCC chairman, said recently. The committee, composed mainly of physicians, will introduce the proposal by means of a citizens petition, "so the dialogue on this important issue can continue in an appropriate manner," he said. Package labeling as well as publicity campaigns of the type HHS launched to warn about Reye Syndrome will be addressed in the petition.

The committee was organized to oppose what it deemed to be "premature" warnings about an aspirin-Reye association, and will work with the government now to avoid premature warnings in the future, Eichenwald said.

The committee is also producing a Reye Syndrome brochure which pediatricians may distribute in their practices. The brochure will help parents recognize the early stages of Reye Syndrome, Eichenwald said. "Until we know what causes it," he said, "the best protection we have is early detection."

Fotografía cortesía de Dolores Mendez-Cashion, M.D.



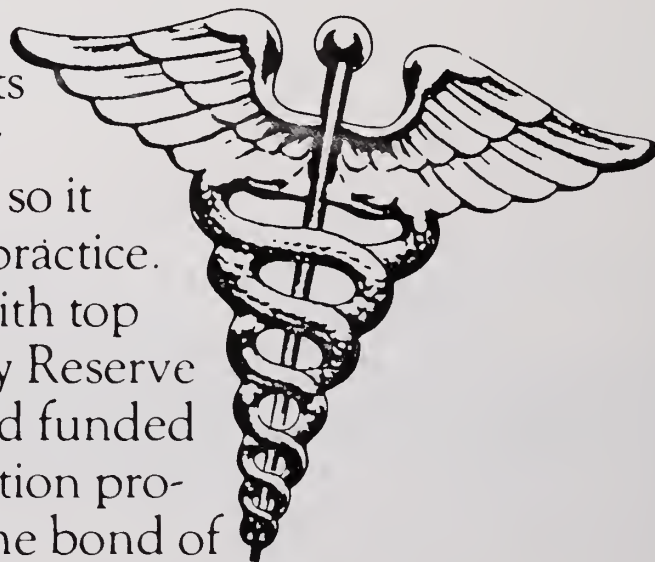
*Escena del Encuentro con los Británicos en 1798.*

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## CDC STUDY SHEDS NEW LIGHT ON KAWASAKI SYNDROME

New data from the Center for Disease Control (CDC), Atlanta, demonstrating a seasonal variation in the incidence of Kawasaki syndrome, suggest that some cases of this mysterious disease may be caused by a microorganism or environmental toxin that is most prevalent in the late winter and spring.

The CDC report in the March 1983 issue of the *American Journal of Diseases of Children* describes an analysis of 523 cases identified from July 1976 to December 1980 through the CDC's National Kawasaki Syndrome Surveillance System and through investigations of suspected outbreaks in New York City; Rochester, New York; Boston; and Honolulu.

Kawasaki syndrome was first described in 1961 in Japan and has been studied in the United States only since 1976. The most susceptible children, according to David M. Bell, M.D., primary author of the CDC report, are of Asian ancestry, male and younger than five years of age. Bell and colleagues also found a significantly higher incidence in black children compared with white children.

The primary features of Kawasaki syndrome are a fever that lasts five days or more; rash; reddening, swelling or peeling of the hands and feet; changes in the membranes lining the mouth and covering the eye; and enlarged lymph nodes in the neck. Bell's group found that the most frequently reported complications were arthritis and other joint problems, irregular heart function and coronary artery aneurysms. The mortality rate among the children they studied was about one percent.

The CDC has been unable to identify a causal infectious agent in Kawasaki syndrome, Bell says. Although the disease shares certain clinical similarities with toxic shock syndrome, such as fever, rash, cardiac problems, and peeling of the extremities, less than one percent of the patients in the CDC study had infections with the *Staphylococcus aureus* bacterium, which has been recognized as the agent responsible for toxic shock syndrome.

The finding that Kawasaki syndrome occurs most often between February and May and the occurrence of localized outbreaks points the finger of blame toward a seasonal infectious agent or environmental toxin, Bell suggests. More recent CDC data have disclosed an apparent association with use of a rug shampoo in patients' homes.

But individual susceptibility is likely to be an important factor as well, Bell warns, since the incidence of Kawasaki syndrome varies with race and sex. In addition, the disease does not seem to be transmissible from person to person or to be related to a common source of exposure, even during community outbreaks.

## ACUTE RHEUMATIC FEVER: DISAPPEARING IN THE U.S.?

Acute rheumatic fever and rheumatic heart disease, once dread complications of streptococcal throat infections in children, may be disappearing in the United States. And if that's the case, according to three physicians writing in a issue of JAMA, it may be necessary to reevaluate current practices for diagnosing "strep throat" and treating rheumatic fever.

Mack A. Land, M.D., and Alan L. Bisno, M.D., from the University of Tennessee Center for the Health Sciences, Memphis, studied acute rheumatic fever in the Memphis area from 1977 through 1981 and found that the incidence among suburban white children aged 5 to 17 years was less than one case per 200,000 population annually. The disease was more prevalent among black children and teenagers in inner-city areas, where the annual rate was 3.74 cases per 100,000 population. The overall rate was 0.64 cases per 100,000 population.

Acute rheumatic fever in Memphis, the authors note, "remains primarily a disease of socioeconomically deprived black to white cases was 5:1."

Land and Bisno only speculate about the reasons why acute rheumatic fever is nearing extinction in the middle-class, largely white suburbs they studied. Several factors, such as improved living standards, decreased household crowding, wider use of antibiotic therapy for respiratory infections and a possible decrease in the virulence of the streptococcal bacteria that cause the disease, may all have contributed to its striking decline.

Their findings, if confirmed in other areas of the country, may have major implications for the diagnosis and prevention of acute rheumatic fever, the authors say. Land and Bisno contend that vigorous attempts to eradicate streptococcal infections in middle-class residential neighborhoods where the disease has become a rarity may no longer be necessary. Although they say that use of throat cultures to screen for the disease on a community-wide basis should be limited to areas still at higher risk, the authors remain squarely behind the throat culture as the best approach to primary prevention of acute rheumatic fever.

An additional benefit of using the throat culture on a case by case basis is that it "effectively rules out strep throat and thus avoids unnecessary administration of antibiotics to the great majority of patients with sore throats who are suffering from an acute viral infection," write Land and Bisno.

In addition, the customary life-long treatment with antibiotics of patients who have had a rheumatic fever attack may not be necessary in all cases, they say.

In an accompanying editorial, Gene H. Stollerman, M.D., from Boston University Medical Center, agrees with Land and Bisno's assessment of the value of the throat culture. "What is required, then," according to Stollerman, "is for such a simple test to be made cost-effective."

Because much of the world's remaining rheumatic fever appears to be caused by a limited number of streptococcal bacterial strains, Stollerman expresses optimism that an effective vaccine may be developed.

### CIGARETTE SMOKE CONTRIBUTES TO CHILDREN'S EAR DISEASES

Children whose parents smoke are more likely to develop chronic middle ear disease than those who live in smoke-free homes, according to a group of Seattle physicians writing in a February 1983 issue of JAMA.

The team of researchers, headed by Micheal J. Kraemer, M.D., from the Division of Allergy at Children's Orthopedic Hospital and Medical Center, Seattle, compared a group of children hospitalized for tympanostomy-tube insertions due to persistent middle-ear effusions with a control group of children hospitalized for other reasons. The groups were matched for age, sex, racial background, family size, household exposure to cigarette smoke, and frequency of catarrh (nasal congestion) and middle ear infections (suppurative otitis media).

The authors found three factors involved more often in children with persistent middle-ear effusions (PRMEE): catarrh, exposure to household cigarette smoke and atopy.

The authors noted that nearly all the hospitalized children with PMEE had had one or more previous episodes of otitis media while only 59 percent of the control group had had similar episodes. Frequent ear infections sharply increase the risk for persistent effusions, according to the authors, and the risk is greatest when all three factors are present.

"Exposure to two or more household cigarette smokers increased the risk for PMEE nearly three fold. With household exposure to smoke from more than three packs of cigarettes per day, the risk increased four fold," Kramer writes. "Children with all three factors —nasal congestion, cigarette smoke exposure and atopy —were more than six times as likely to manifest PMEE."

In the same JAMA issue, a group of researchers headed by David W. Teele, M.D., from the Department of Pediatrics, Boston University School of Medicine, reported that a substantial portions of pediatric visits are due to diseases of the middle ear.

The authors analyzed data about 2,570 children followed from birth and found that during the first year of life 22.7 percent of all physician visits involved middle ear disease; for two —and three-year-olds, 33.9 percent and 34.6 percent respectively, and for four— and five-year-olds nearly 40 percent of visits were because of middle ear disease. They also note that about one in three visits made for illness of any kind resulted in a diagnosis of middle ear disease.

The Boston team suggests that "any intervention to decrease the incidence of acute otitis media or to hasten the resolution of middle ear effusions would substantially reduce the costs of providing care to children."

### STUDY SHOWS BIRTH DEFECT RISK REMAINS HIGH FOR OLDER WOMEN

New data gathering techniques developed at the New York State Department of Public Health support previous studies showing that birth defect rates for fetuses of would-be mothers who are 45 years old are ten times higher than the rates seen for fetuses of 35-year-old women.

The chance of 35-year-old woman having a live born child with a chromosomal abnormality is 5.0 per 1,000 births; at 40 years of age the rate increases to 15.0 for every 1,000 births; and at age 45 the risk spirals upward to 50.0 for every 1,000 births, say Ernest Hook, MD, and colleagues in the April 25, issue of JAMA. The authors are affiliated with the New York State Department of Health and Albany Medical College.

The researchers estimate that the incidence of Down's Syndrome, the most prevalent birth defect in infants born alive, remains unchanged from rates recorded between 1963 and 1974.

Also known as mongolism, Down's Syndrome is a genetic disorder characterized by certain physical anomalies and varying degrees of mental retardation.

The pediatricians believe that their new statistical method of combining amniocentesis data with natural history data of a fetus produces accurate birth defect rate estimated for live births.

"These are rates in live-born infants that would be predicted if selective abortion following prenatal diagnosis did not occur," the report says. "Because they are derived from more recent data and involve fewer assumptions in derivation —being based on direct studies— these rates provide, in our view, more reliable estimates pertinent to contemporary genetic counseling of risks in live-born infants than those published earlier."

This statistical model will prove more valuable in predicting defect rates among older women as contraception, prenatal diagnosis and voluntary abortion continue to reduce live birth rates.

### HIGH SCHOOL FOOTBALL PLAYERS AT RISK FOR ASEPTIC MENINGITIS

A new study by researchers at the Centers for Disease Control indicates that high school football players appear to be vulnerable to aseptic meningitislike illness (AMLI).

Melinda Moore, MD, and colleagues investigated seven outbreaks of AMLI during 1978 and 1980 that occurred in young football players in four different states.

Two high schools in North Carolina were affected, with nine cases of aseptic meningitis occurring primarily among varsity football players at one school, and seven cases among football players at another.

A total of 12 cases were reported from high schools at two locations in New York State; nine football players from high schools at two locations in Missouri were hospitalized, and four from a high school located in Ohio were hospitalized.



Aseptic meningitis is a relatively mild form of the disease caused by enteroviruses that attack the gastrointestinal tract.

"Surveys conducted at these seven schools suggested that attack rates of AMLI were higher among football players than among other student athletic teams," the researchers say. "The high attack rates of AMLI in football players, indicating an unusually high case-infection ratio, support the concept that such players may indeed be at greater risk. Moreover, the higher rate of hospitalization for AMLI among football players also suggests their illness was more severe," they add.

The researchers speculate that four factors may be involved in the unusual outbreaks of AMLI among high school players. First the time of year that football players assembled as a group for season practice coincided with the peak of the enterovirus season.

Second, the physical contact among football players was probably closer than among other students, increasing the opportunity for transmission of enterovirus. Third, unhygienic sharing of team water bottles during practice may have been a factor. Fourth, greater physical exertion may have predisposed the youthful football players to AMLI instead of a milder enterovirus infection.

The CDC researchers caution high school football teams to provide single-use paper cups for drinking water. They also suggest that players avoid dipping hands or cups into the team's water container.

### WHEN INTENSIVE CARE DOESN'T HELP

Physicians must make difficult medical, economic and ethical decisions when choosing whether or not to admit a critically ill patient to an intensive care unit (ICU). The dilemmas they face—and their frustration when the most vigorous medical care cannot prevent a patient's death—are highlighted in two contributions to a recent issue of JAMA.

In a study to investigate the effect of ICU care on the outcome of blood infection with pneumococcus bacteria, Edward W. Hook III, MD, from the University of Washington, Seattle, reports that mortality from the disease, called pneumococcal bacteremia, has remained unchanged over the past 20 years despite major advances in the life-support measures offered in ICUs. The precise mechanism by which pneumococcal bacteremia causes death is unknown.

Hook studied 134 consecutive cases of the disease over a six-year period. Mortality was 30.5 percent overall and 76 percent among patients admitted to the intensive care unit. The 30.5 percent mortality is not substantially different from rates of 25 percent and 28 percent reported by other investigators in studies published in 1964 and 1974, respectively, Hook says.

"Patients requiring intensive care for the disease rarely survive", according to the author. "The physiological consequences of pneumococcal bacteremia may have been delayed or modified by ICU care, but the ultimate outcome was probably determined by events occurring early in the course of infection." The findings associated with the highest mortality were the same as those reported in the earlier studies, Hook found: a reduced white blood cell count, advanced age, preexisting malignancy or other chronic complicating disease, and presence of pneumonia in two or more lobes of the lungs.

The major effect of ICU care demonstrated in Hook's report was the delay of death from early to later in the hospitalization. Only 27 percent of the patients he studied died within 24 hours of admission to the hospital, compared to 43 percent reported in the 1964 study.

Hook's study "highlights a widely held misperception of the ability of ICU therapy to save lives by correcting physiological abnormalities", writes William A. Knaus, MD, from the George Washington University Medical Center, Washington, D.C., in an accompanying editorial. "The best that good ICU care can accomplish is to reverse acute physiological abnormalities and buy time. If, during this time, therapy works or the body mounts its own attack, the patients will live. If not, then all ICU care can achieve is a delay," Knaus says.

ICU care reduces the immediate risk of death for a wide range of acute illnesses and has been shown to be effective in improving the outcome for burn patients, Knaus concedes. But "if we accept ICU care as life support, it is clear that not everyone who becomes acutely ill belongs in an ICU. Patients with chronic incurable diseases or an irreversible acute process should not be admitted. But how can physicians identify these patients?" Knaus asks.

Scientific study of acutely ill patients could help identify which of the body's reactions to disease are most likely to benefit from ICU care, according to Knaus. Physicians could use these physiological and clinical indicators in deciding whether or not to admit a patient to an ICU. Such research might also spot warning signs that could prompt earlier, perhaps life-saving, ICU admission, he speculated.

No amount of research will completely eliminate the uncertainty that now makes ICU admission a difficult medical and ethical decision, Knaus says. "We should recognize, however, that the response to this uncertainty should not be more ICU's, but more knowledge".

Intensive care unit financial costs now account for nearly one percent of the gross national product of the United States, according to Knaus. Research efforts should aim at defining both the capabilities and the limits of this expensive medical intervention, he advises.

### TEEN PREGNANCY NOT ALWAYS HARMFUL TO FETUS

Although teenage pregnancy is considered a major social problem in the United States, the newborns of teenage mother are not necessarily less healthy than those of older mothers, according to two University of Michigan researchers.

Newborns and infants of teenage mothers, although often weighing less than offspring of mothers in their 20s, actually score higher on some tests of early physical and mental development writes Stanly M. Garn, PhD, and Audrey S. Petzold, from the university's Center for Human Growth and Development, in the April issue of *American Journal of Diseases of Children*.

Garn and Petzold analyzed the effects of maternal size, weight and maturity on birth outcome from data collected on 11,464 teenage participants in the National Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke. They compared their findings with additional data on outcomes for pregnant

women aged 20 to 29 and with data on nonpregnant teenagers.

The authors found teenage mothers to be small, averaging about five feet in height and 115 pounds in weight at the age of 13.5 years. Although smaller and lighter than pregnant women in their 20s, they were comparable to nonpregnant girls of the same age. The teenage mothers had also started menstruating at an earlier age than women who became pregnant in their 20s.

Through statistical analysis, Garn and Petzold found that even though teenagers give birth to many low-birthweight infants, the relationship between the mother's weight at conception and the birth weight of her baby was the same for both teenagers and older mothers—that is, smaller women and smaller babies, regardless of age. The authors concluded, then, that newborns of teenage mothers were small because of maternal size rather than age.

Although birth weights increased with maternal age from

13 through 19 and into the 20s, their children up to the age of seven years showed no difference in weight regardless of how old their mothers were at conception.

In addition, Garn and Petzold found that both newborns and eight-month-old infants of teenage mothers scored higher on tests of physical, neurological and mental development than those of older mothers. In fact, the incidence of lower scores on these tests increased with maternal age each year from 13 to 19 years and older.

Taking these findings into consideration, say the authors, "teenage pregnancies cannot be viewed as a biologic disaster."

Even though larger weight gains during pregnancy lead to higher birth weights, the authors do not recommend that teenage mothers gain more than about 31 pounds. More weight may not benefit the mother, they say, and will have less influence on the weight of the newborns than additional weight has on infants of older women.

Fotografía cortesía de Dolores Mendez-Cashion, M.D.



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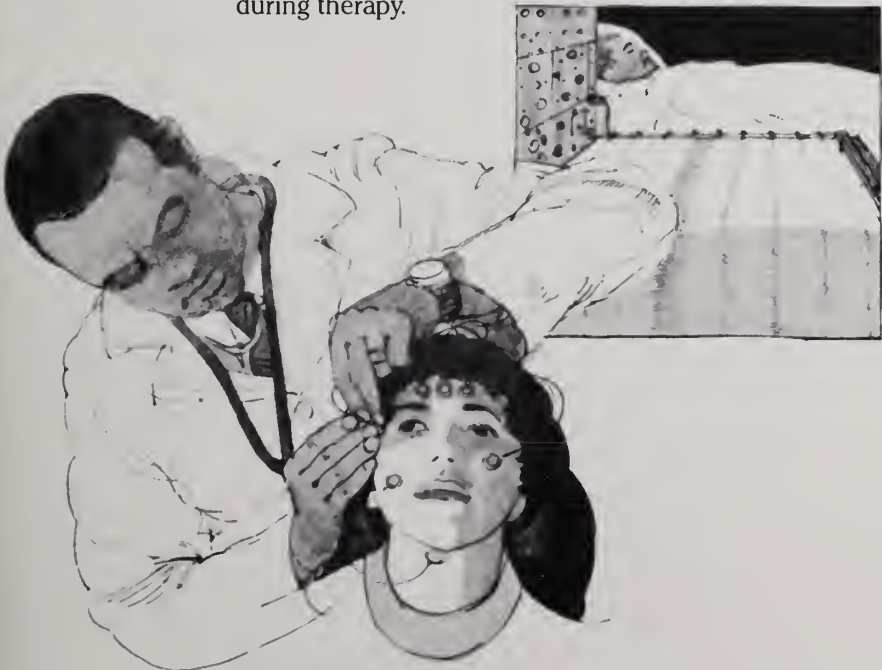


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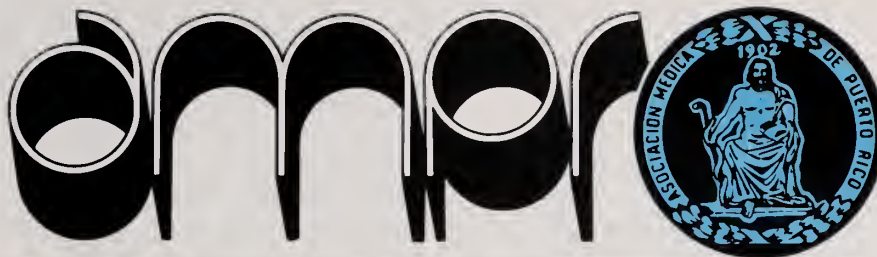
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# Columna del Editor



Con este número se cumple un año y medio de trabajo por la Junta Editora actual. Para esta época el año pasado confrontábamos el problema serio de insuficientes anunciantes, no teníamos una impresora eficiente y los artículos científicos de calidad adecuada para publicación eran escasos. Como consecuencia de esto nos vimos obligados a combinar los números de junio y julio en uno solo y no fue hasta octubre que pudo aliviarse esta crisis. Hoy, un año más tarde hemos resuelto el problema de la imprenta y puede apreciarse la mejoría gráfica y calidad de impresión en cada número. Las fotografías a color en los últimos dos números así lo atestiguan. Por otro lado los anunciantes locales han compensado algo el vacío económico creado por la ausencia de los anunciantes norteamericanos y, aunque a ritmo lento, se siguen recibiendo colaboraciones científicas para su consideración.

El contenido de este número es muy variado. Comienza con el Pathology Review de la Dra. Castillo quien nos presenta un artículo sobre el sarcoma de Kaposi con ilustraciones a color de lesiones cutáneas en esta enfermedad por el síndrome de inmunodeficiencia adquirida (AIDS). Le sigue un artículo sobre la enfermedad de Hodgkins por la División de Radioterapia Oncológica del Hospital Universitario y un trabajo corto de Obstetricia, especialidad que por primera vez en varios años publica un artículo en nuestra revista. Reaparece en este número el Foro de Medicina Nuclear, ausente desde enero de 1982 y "revivido" gracias al esfuerzo del Dr. Julio V. Rivera y sus colaboradores del Hospital de Veteranos. Hay además varios Artículos de Repaso de calidad y un Artículo Especial sobre el uso de psicofármacos en Psiquiatría el cual es sin duda de gran utilidad práctica.

Creemos que la revista continuará su curso estable en los tres aspectos mencionados anteriormente, que son vitales para su publicación y en los cuales venimos trabajando a diario por año y medio.

Rafael Villavicencio, M.D.  
Presidente Junta Editora  
Boletín Asociación Médica de Puerto Rico

ASOCIACION MEDICA DE PUERTO RICO

## BOLETIN



VOL. 75/NUM. 6

JUNIO 1983

### NUESTRA PORTADA:

Mujer con Peces, óleo sobre masonite de Rubén Moreira.

El artista nació en Fajardo en 1922. Estudió en los Estados Unidos en Cooper Union Pratt Institute y la Grand Central School of Art. Fue discípulo de Harvey Dunn. En 1957 después de varias visitas a su país, regresa para quedarse en Puerto Rico. Exhibe en la Galería Campeche, en el Ateneo y el Instituto de Cultura Puertorriqueña. Ha recibido premios del Ateneo Puertorriqueño y el Colegio de Abogados. Ha hecho murales entre los cual se destacan los paneles para la Biblioteca del Hospital de Siquiatría en Ponce. Ha sido también profesor en la Escuela de Artes Plásticas del Instituto de Cultura. Esta representado en varias colecciones entre las cuales están las del Ateneo, la del Instituto de Cultura y en varias otras públicas y privadas. Como artista gráfico ha expuesto en muchas exposiciones en el país, en especial la Sala de Artistas Gráficos Puertorriqueños.

La reproducción de la obra en nuestra portada ha sido posible gracias a la gentileza del autor y del Taller-Galería André en el Condominio el Centro en Hato Rey, donde actualmente se encuentra expuesto el óleo.

# EDITORIAL



## Uso de Drogas Contraceptivas en Pacientes Cardíacas

Después de 17 años de experiencia atendiendo semanalmente, en carácter de Supervisor de estudiantes de post-grado, en una de las pocas clínicas en la nación americana de embarazadas con problemas de alto riesgo cardiovascular, hemos llegado a las siguientes conclusiones sobre el uso de terapia contraceptiva en pacientes cardíacas.

La experiencia nos ha demostrado, que estaríamos de acuerdo en usar una terapia contraceptiva en tanto una paciente se pone en condiciones óptimas para proceder a cirugía cardíaca rehabilitadora. Esto incluye a toda paciente clase II, en la clasificación funcional de la Asociación del Corazón de Nueva York, o sea dicho, pacientes con lesiones cardíacas no cianóticas que tienen síntomas el esfuerzo máximo. También a las clase III que, con terapia y estricta vigilancia se han tornado II y ya no se diga las que caen en la clasificación funcional I, en todas éstas usaríamos la llamada "pildora".

Ahora bien, es nuestro parecer, que no se debe usar una terapia contraceptiva en los siguientes casos:

1. Pacientes cardíacas reumáticas con fibrilación auricular debido al peligro de trombosis. Aunque este servidor y el Dr. Roberto Rodríguez Estapé, revisamos un gran número de fibriladoras crónicas reumáticas y pocas de ellas tuvieron fenómenos embólicos, preferimos que éstas no usen terapia contraceptiva.
2. Pacientes cardíacas con insuficiencia congestiva crónica; sabemos que estas pacientes tienen propensión a fenómenos embólicos, así que no podemos añadirles un riesgo más.
3. Pacientes de post-cirugía y en anticoagulantes con reemplazo de válvula; esto se ampliaría hasta pacientes con reemplazo de válvulas porcinas, aunque se sabe en éstas hay menos incidencias de embolias.
4. Pacientes con un historial de embolia pulmonar recurrentes o tromboflebitis profundas frecuentes porque se han

descrito trastornos similares con el empleo de terapia contraceptiva en mujeres normales y no se recomiendan en aquéllas que ya han sufrido estos trastornos.

5. Pacientes con enfermedades congénitas cianóticas, sobre todo en aquéllas cuyo hematocrito sea mayor a 45%, pues en éstas hay mayor propensión a abortos espontáneos, embolias y a neonatos de bajo peso.
6. Pacientes con enfermedad congénita e hipertensión pulmonar. Estas pacientes de por sí, son un alto riesgo y no vamos a añadirle a una vida ya comprometida más variantes.
7. Múltiparas con venas varicosas en ambas extremidades inferiores y en sus órganos genésicos. La razón es contundente, pues casi siempre estamos frente a mujeres mayores, pasados los 35, a las que no vamos a recomendar terapia contraceptiva. Las varicosas y la terapia contraceptiva predisponen a tromboflebitis y fenómenos embólicos, literatura que nos plagó en los años 60 y 70.
8. Pacientes con hipertensión arterial. Han aparecido suficientes artículos en la literatura mundial, asociando la terapia contraceptiva a hipertensión arterial. A una mujer en edad reproductiva con hipertensión sería crearle más problemas. En esto somos estrictos; no aceptamos terapia contraceptiva y terapia antihipertensiva.
9. Pacientes con prolapso de válvula mitral sintomática. Sabemos que hay un número considerable de mujeres con prolapso de válvula mitral asintomático, que antes de la era del ecocardiograma quizás llamábamos insuficiencia mitral o soplo funcional. A una paciente con palpitaciones, dolor de pecho, mareos, con o sin hallazgos clínicos y un estudio electrocardiográfico que puede ser positivo o negativo, después que tengan síntomas no le recomendamos una terapia contraceptiva por la incidencia pequeña, pero conocida, de fenómenos embólicos.

Hay una condición que no es cardíaca sino hematológica, pero que por tener repercusión cardiopulmonar, la añadimos a nuestra lista de contraindicaciones. Esta es la Anemia Depranocítica ("Sickle Cell Anemia"), ya que sabemos que hay fenómenos embólicos creados por los cuerpos tactoides in situ y no vamos a añadirle a estos seres, otro factor de riesgo.

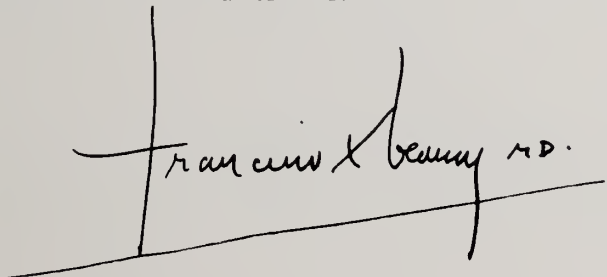
Esta es la experiencia de 17 años de trabajo con pacientes cardíacas embarazadas. Nosotros, en esto somos más condescendientes que otros compañeros de la Literatura Médica Americana, ya que ellos proponen que no se use ningún contraceptivo oral en cardíacas, pero nosotros creemos que si



a estas pacientes se les está preparando para hacerles una cirugía cardíaca rehabilitadora, sí amerita su uso.

Recomendamos una terapia de contraceptivos orales en mujeres jóvenes, delgadas, de una vida activa y que no tengan el vicio del tabaquismo. Son muchas las mujeres que después de una terapia contraceptiva y de una cirugía cardíaca, hoy en día están completamente rehabilitadas y llevan una vida normal.

Además, conviene no olvidar, que fue en Puerto Rico en donde el doctor Gregory Pincus usó por primera vez la terapia contraceptiva y nosotros hemos podido estudiar los casos de algunas de estas primeras pacientes. Sería sumamente interesante considerar desde distintos ángulos de investigación, algunos de estos casos y sería algo señero en la historia de la salud en Puerto Rico.



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## AGRADECIMIENTO

La utilización de papel cromado en este número del Boletín ha sido posible gracias a una donación del Distrito Este de la Asociación Médica de Puerto Rico.

La Junta Editora del Boletín de la Asociación Médica le agradece al Presidente del Distrito Este, el Dr. William Matos, y a su Junta de Directores el interés demostrado en el mejoramiento de nuestro órgano oficial.







# The labyrinth of the lung

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## Alupent<sup>(R)</sup> Tablets

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and 20 mg

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## Bronchodilator

Please see following page for brief summary of prescribing information, including warnings, precautions, and adverse reactions.

The labyrinth of the lung...  
a sculptural representation  
of the microscopic terminal  
airways, respiratory bronchioles  
and alveolar ducts

# The labyrinth of the lung

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##### Bronchodilator

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**Information for Patients:** Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

**Carcinogenesis:** Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed.

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no teratogenic or embryocidal effect at 50 mg/kg, or 310 times the human inhalation dose and 31 times the human oral dose. There are no adequate and well-controlled studies in pregnant women. Alupent, brand of metaproterenol sulfate, should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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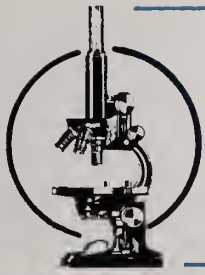
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## Sarcoma de Kaposi

El Sarcoma de Kaposi es un tumor vascular multicéntrico que se manifiesta con nódulos hemorrágicos en la piel y otros órganos. Es más frecuente en hombres que en mujeres en una proporción de 9 a 1 y las manifestaciones clínicas dependen de la distribución geográfica de la enfermedad y del estado inmunológico del paciente. Recientemente hemos notado la asociación de una variante agresiva, rápida y fatal de sarcoma de Kaposi con infecciones oportunistas en pacientes sin historial previo de condiciones que afectan su sistema inmunológico.

“AIDS” son las siglas que identifican en inglés el nuevo síndrome de inmunodeficiencia adquirida que acarrea una alta tasa de mortalidad y que afecta primordialmente a hombres jóvenes homosexuales, adictos a drogas, hemofílicos y haitianos.

Ya que las manifestaciones clínicas del sarcoma de Kaposi, asociado con el síndrome de inmunodeficiencia adquirida, son diferentes a las del llamado sarcoma de Kaposi clásico, queremos presentar las dos variedades:

- La variante clásica del sarcoma de Kaposi ocurre en Europa y Norte América. Se manifiesta con lesiones indolentes, rojiza-marrón, en la piel, predominantemente de las extremidades inferiores. La enfermedad es de una evolución lenta de tres a cuatro años con una incidencia que hace el 0.02% de todos los tumores malignos en los Estados Unidos de Norte América. En Europa afecta más frecuentemente a personas del sur de Europa, de los países mediterráneos y de descendencia judía. Algunos autores llaman a esta variedad, Mediterránea. Su presentación clínica es igual a la que ocurre en Norte América y se le llama Sarcoma de Kaposi Clásico pues se ajusta a la primera descripción de la enfermedad publicada por el Dr. Moriz Kaposi en 1872.

- En el África, particularmente en los países de la zona ecuatorial de dicho continente, ocurre una variante que afecta la población negra de esa región. La enfermedad se manifiesta de forma diferente en niños y en adultos, y representa del 3% al 9% de todos los tumores malignos que ocurren en esa zona. El sarcoma de Kaposi de niños africanos se caracteriza por el involucramiento masivo de los ganglios linfáticos y órganos internos y en su evolución semeja un linfoma. La variante africana es de una evolución rápida y fulminante con un curso clínico de un año aproximadamente. Estos casos responden a la quimioterapia con dramática desaparición de los nódulos. En adultos la variedad africana tiende a ser cutánea-nodular con extensión a la dermis y a los huesos.

La relación de sarcoma de Kaposi, con alteraciones de supresión del sistema inmunológico, empezó a notarse en pacientes que habían recibido transplantes renales y drogas inmunosupresoras incluyendo corticosteroides. Muchos de estos pacientes manifiestan mejoría y desaparición de las lesiones cuando se discontinúa la terapia de inmunosupresión, lo que hace pensar que el sarcoma de Kaposi es un reflejo de la alteración de la respuesta inmunológica.

También hay que hacer notar la peculiar asociación del sarcoma de Kaposi con otros tumores malignos ocurriendo en pacientes que ya presentan una malignidad, particularmente si son malignidades linfocitales como los linfomas.

La variante clínica del sarcoma de Kaposi, asociada al síndrome de inmunodeficiencia adquirida que afecta a adultos jóvenes homosexuales sin historial previo de enfermedades del sistema inmune, se parece más a la variante africana que a la variante clásica. Esta variante ocurre en pacientes con infección previa o concurrente por *citomegalovirus* y *pneumocistis carinii*. Otros organismos encontrados son virus de herpes, candida, bacilos tuberculosos atípicos y otros considerados “oportunistas”.

La aparición de esta variante del Sarcoma de Kaposi, ha tomado proporciones epidémicas en los Estados Unidos de Norte América desde mediados del año 1981. Al presente hay documentados más de 500 casos en un período de dos años.

La mayoría de estos pacientes presentan alteración de la respuesta inmuno-celular con anormalidades de las funciones de los linfocitos T, demostrándose una mayor proporción de las células supresoras sobre las células T citotóxicas al igual que una disminución en el número de los linfocitos T accesorios (ayudantes).

La causa de las alteraciones de las células inmunoreguladoras desconoce pero se piensa que la infección con el citomegalovirus u otro virus podría ser el mecanismo que desencadene este fenómeno. La asociación del sarcoma de Kaposi y este virus fueron descritas por primera vez por Giraldo en 1975.

Las manifestaciones cutáneas del sarcoma de Kaposi clásico varían desde placas dermales, pápulas, nódulos y tumores. Las lesiones empiezan como una pequeña mancha o pápula rojiza-azulada que según envejece se torna marrón. Las lesiones, que varían de una a varios cientos, tienden a confluir y se presentan en varios estadios. (Fig. 1).

Las pequeñas pápulas progresan a placas, nódulos y tumores que a veces presentan un aspecto verrucoso y fungante con tendencia a la ulceración. Las lesiones son más comunes en las extremidades inferiores y están acompañadas de edema, hemorragias espontáneas y dolor que impiden caminar. Las lesiones ocurren más tarde en el pecho, cuello, genitales, cabeza o cualquier área de la piel.

Los órganos internos afectados incluyen pulmones, hígado, riñones, tracto gastrointestinal, mucosa oral, pericardio, ganglios linfáticos y adrenales.



Fig. 1. Lesiones cutáneas de sarcoma de Kaposi variedad clásica.

Las manifestaciones cutáneas del sarcoma de Kaposi, asociado con el síndrome de deficiencia inmunológica adquirida (AIDS), son diferentes. Estas lesiones no aparentan tener predilección por ningún área corporal. Aparecen como pápulas o placas pequeñas violáceas, de 1 a 1.5 cm., alargadas, con apariencia de cigarro (Fig. #2), en la piel de la cara, párpados, espalda, pecho, y genitales. No presentan tendencia a confluir y aparecen después de un período variable de tres semanas a seis meses de fiebre, pérdida de peso, debilidad, neumonía, linfadenopatía e infecciones oportunistas.

### Patología

El diagnóstico de sarcoma de Kaposi se establece por biopsia de las lesiones cutáneas. En la piel, el tumor ocurre en la zona media e inferior de la dermis dejando una banda de tejido normal entre la epidermis y el tumor. (Fig. #3). Cuando la lesión progresa la epidermis se ulcera.

Histológicamente las lesiones del sarcoma de Kaposi se caracterizan por la presencia de canales vasculares tapizadas por células endoteliales malignas (Fig. #4) y un estroma de tejido conjuntivo de células fusiformes que representan fibroblastos malignos. Estas células pueden formar haces estromales o también tapizar lechos vasculares. Hay depósito de hemosiderina intra y extracelular y un componente inflamatorio que parece tejido de granulación.

Hay variantes histológicas de menor a mayor anaplasia y las lesiones pueden parecer hemangiomas capilares benignos y en ocasiones se necesitan varias biopsias para llegar a un diagnóstico definitivo.



Fig. 2. Lesión cutánea de sarcoma de Kaposi en paciente con el síndrome de inmunodeficiencia adquirida (AIDS).



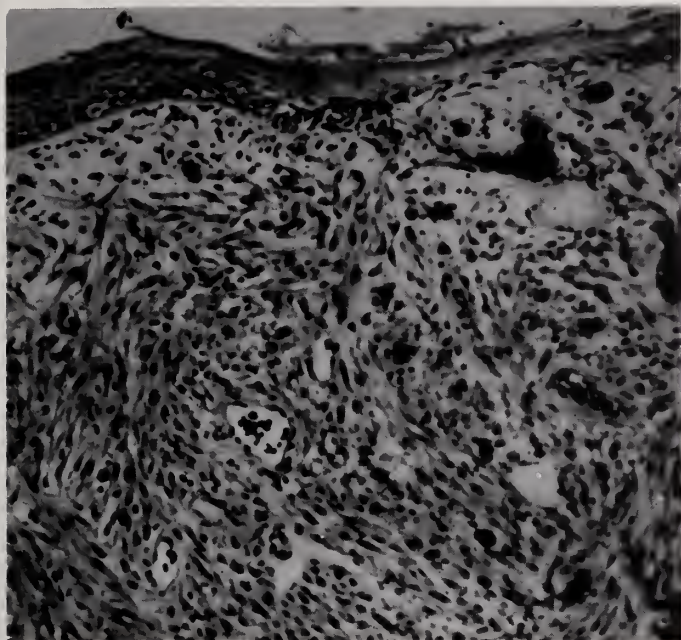


Fig. 3. Biopsia de piel, sarcoma de Kaposi compuesto por canales vasculares y un estroma fibrosarcomatoso.

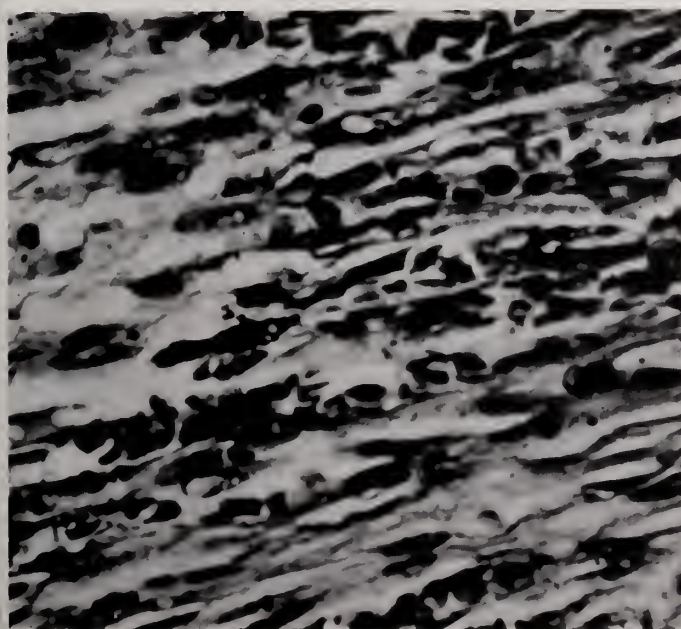


Fig. 4. Sarcoma de Kaposi. Canales vasculares tapizados por células endoteliales malignas.

La determinación del factor VIII de coagulación por el método de inmunoperoxidasa en tejido parafinado se utiliza para determinar que las lesiones del sarcoma de Kaposi son de origen endotelial.

Los tumores que ocurren en los ganglios y órganos internos presentan las mismas características histológicas que las lesiones cutáneas.

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**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. Note: The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.

For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.

For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

Also for the treatment of documented *Pneumocystis carinii* pneumonitis.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term; nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age.

**Warnings:** BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL PHARYNGITIS. Clinical studies show that patients with group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, hepatocellular necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions:** General: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin; reassess coagulation time when administering Bactrim to these patients. **Pregnancy:** Teratogenic Effects: Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folic acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, hepatocellular necrosis, diarrhea, pseudomembranous colitis and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, epathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diabetes and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for infants less than two months of age.

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

**Children:** Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours. In two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

**For patients with renal impairment:** Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

**ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS:**

**Usual adult dosage:** 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 14 days.

**PNEUMOCYSTIS CARINII PNEUMONITIS:**

Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 20. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40. Pediatric Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); cherry flavored—bottles of 100 ml and 16 oz (1 pint). Suspension, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per tea spoonful (5 ml); fruit-licorice flavored—bottles of 16 oz (1 pint).



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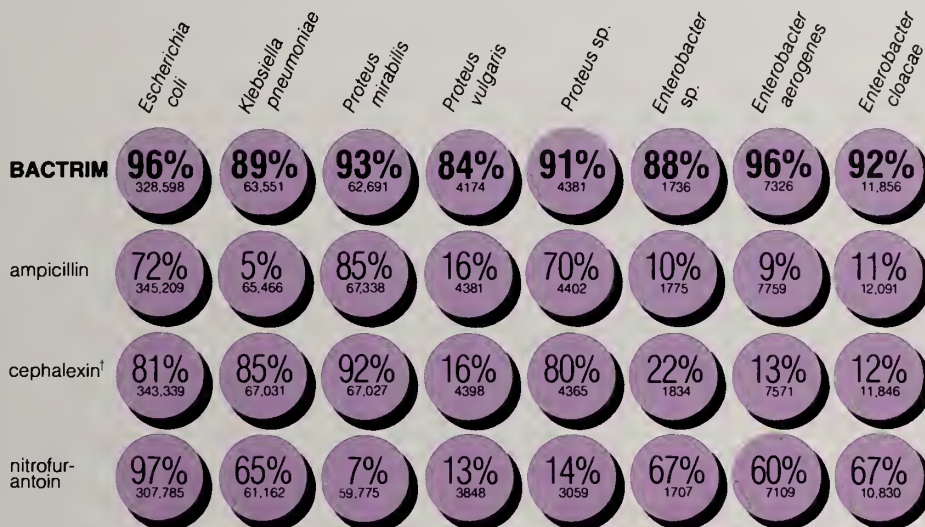
In vitro studies demonstrate



# Bactericidal activity

## with minimal resistance

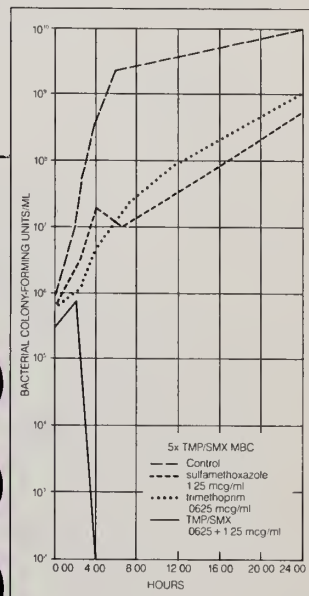
Percent of isolates of common uropathogens sensitive to BACTRIM and to other antimicrobials



<sup>†</sup>Analogous to cephalothin, the primary antibiotic disc used in testing.

Source: The Bacteriologic Report, BAC-DATA Medical Information Systems, Inc., Winter Series, 1981-82. Numbers under percentages refer to the projected number of isolates tested.

RAPID IN VITRO DESTRUCTION OF *E. COLI*\*



Kill curve kinetics of Bactrim and its individual components against *E. coli* in vitro.<sup>1</sup>

The bactericidal action of Bactrim has been demonstrated *in vitro* on laboratory strains of *E. coli*<sup>1,2</sup> and on clinical isolates of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis* and *Morganella morganii*<sup>3</sup>—the most common causative organisms of urinary tract infections.<sup>4</sup> More than 100 published studies attest to the efficacy of Bactrim in recurrent urinary tract infections due to these organisms.<sup>5</sup> In comparative studies with other antimicrobials, Bactrim has consistently demonstrated unsurpassed efficacy during therapy.<sup>6-11</sup>

Resistance to Bactrim develops more slowly than to either of its components alone *in vitro*.<sup>\*</sup> Among urinary tract isolates, resistance has rarely emerged in susceptible strains.<sup>5,12</sup> Bactrim is contraindicated in pregnancy at term, during lactation, in infants less than two months old and in documented megaloblastic anemia due to folate deficiency. Initial episodes of uncomplicated urinary infections should be treated with a single-agent antimicrobial.

# Bactrim™ DS

(trimethoprim and sulfamethoxazole/Roche)

b.i.d. for recurrent urinary tract infections

<sup>\*</sup>*In vitro* data do not necessarily predict clinical results.

# Motrin<sup>®</sup>

ibuprofen, Upjohn

## 600 mg Tablets



More convenient for your patients

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# ESTUDIOS CLINICOS

## The Prognostic Value of Staging Laparotomy for Hodgkin's Disease: Experience at the University District Hospital of the University of Puerto Rico

José R. Santana, M.D.  
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**Abstract:** One hundred and fifty-nine patient who presented at the University District Hospital (U.D.H.) from January 1966 to December 1978 with the diagnosis of Hodgkin's Disease were analyzed. Fifty-five percent (88/159) of the patients were submitted to a staging laparotomy. For the purpose of analysis we utilized the clinical staging prior staging laparotomy of the patients with Stage I and II (80 patients) and compared this group with patients with clinical Stage I and II who were not submitted to staging laparotomy (31 patients). Patients with staging laparotomy had 76% five-year survival and those without a staging laparotomy had a 67% five-year survival ( $p=0.37$ ). The disease free survival was 49% for the clinical Stage I and II with laparotomy in comparison to 36% of the Stage I and II without laparotomy ( $p=0.19$ ). The five-year survival for all cases was 72%. Relapse occurred below the diaphragm despite negative staging laparotomy in 10% of the patients reviewed. At this moment it appears that surgical staging represents a method of selecting a sample of patients with early and favorable disease. Our analysis do not show any benefit to exploratory laparotomy for Stage IA and IIA Hodgkin's Disease. We do not recommend it for this group if radiotherapy will involve the para-aortic and splenic areas as standard treatment. The exploration should be limited to Stage IB, IIB and IIIA because they have high risk of unsuspected liver or lymph node involvement outside of the standard radiotherapy fields.

*This work was supported in part by National Cancer Institute Grants: R10CA 12258-10 and CA 16598-07.*

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There has been significant progress in the last few decades in the management of Hodgkin's disease. Many factors have been involved in this progress. The pathological classification of Lukes & Butler,<sup>24 25</sup> and the modification of the same accepted at the Rye International Conference,<sup>26</sup> with its prognostic significance, was a major breakthrough. The staging laparotomy as pioneered by Kaplan and his group at Stanford,<sup>13</sup> the radiotherapeutic management with total nodal irradiation,<sup>20 22</sup> and the use of chemotherapy for Stage IV Hodgkin's disease with MOPP, as developed by Dr. De Vita at the National Cancer Institute,<sup>6 7</sup> have all contributed to progress in the management of this disease.

The staging laparotomy has yielded important information on the natural history of the disease. In 1961, Dr. Kaplan and his group began doing laparotomies for staging of selected patients and normal lymphangiograms, and those with abnormal hepatic function tests or a suspicious lymphangiogram, but no diagnosis, were selectively explored.<sup>13</sup>

In 1969, upon reviewing the data in 65 selected patients with Hodgkin's disease, explored at Stanford, Glatstein found there was a change in stage in 12/37 (32%) of untreated patients with suspected abdominal involvement.<sup>13</sup> They found no liver invasion by Hodgkin's disease without evidence of advanced disease in the spleen. In addition they found that the hepatic function tests and the liver scan were both poor predictors of hepatic involvement by Hodgkin's disease.

In July 1968, Kaplan and associates started a prospective study of splenectomy for unselected cases with Hodgkin's disease. In the analysis of 814 cases<sup>18</sup> they found that laparotomy changed the stage in 31% of patients. The spleen was positive for Hodgkin's disease in 311 patients (38%). Involvement of the spleen by Hodgkin's disease correlated with histopathology ranging from 16% in lymphocytic predominance, to 83% in lymphocytic depletion. The Stanford Group reported that the paraaortic and splenic lymph nodes were positive in 50% of the cases with involvement of the spleen. No operative mortality was noted, but eight major complications occurred in the first 291 laparotomies.

Since the Stanford experience was published, it has been generally accepted that staging laparotomy for Hodgkin's disease is productive, of low morbidity, and associated with almost no mortality.<sup>18</sup>

In 1971 the initial experience with staging laparotomy at the University District Hospital (U.D.H.) was reported. In the first 20 consecutive patients surgically explored for Hodgkin's disease, 11 had a change in stage<sup>29</sup>.

The purpose of this paper is to analyze the experience at the U.D.H. in San Juan with 88 laparotomies for staging of

Hodgkin's disease performed from 1966 to 1978. The final objective is to define the prognostic value of staging laparotomy in the management of Hodgkin's disease in Puerto Rico.

### Material and Methods

One hundred and fifty nine patients who presented at the University District Hospital (U.D.H.) from January 1966 to December 1978 with the diagnosis of Hodgkin's disease were analyzed. The diagnosis of Hodgkin's disease was based on a biopsy performed at U.D.H., or a review of slides from other hospitals. Routine staging procedures included chest radiographs, chemical and hematologic surveys and urinalysis. Lymphangiography, sonography, computerized tomography, and chest tomograms were performed only on selected patients. The Ann Arbor staging system was used.<sup>3</sup> The histopathologic subtypes were classified according to the Rye modification of the Lukes and Butler system.<sup>26</sup> All patients were treated at the U.D.H.

Fifty five percent (88/159) of patients were submitted to a staging laparotomy. Of this group, we analyzed the age distribution, site of initial manifestation, histology, change in stage after surgical staging, complications of surgical staging and abdominal relapses after negative staging laparotomy. For the purpose of analysis, we utilized the clinical staging prior to staging laparotomy of the patients with Stage I and II (80 patients) and compared this group with patients with clinical Stage I and II who were not submitted to a staging laparotomy (31 patients). We determined the characteristics of both groups in turn of B symptom, stage distribution, age distribution and histological distribution. The five year survival was determined for the two groups. The p-values were calculated.

### Results

Age distribution of the 88 explored patients is shown in Table 1; most cases (77%) were in the first three decades of life. There were 47 (53%) adults and 41 (47%) children (defined as less than 18 years of age) who had laparotomy. Fifty-nine were males (67%) and 29 (33%) were females. The site of initial manifestation is shown in Table 2; most patients (76%) had the initial manifestation in the neck. Histology is shown in Table 3; the most common histologies were mixed cellularity (38%) and nodular sclerosis (32%).

The majority of patients (57%) were first treated with irradiation; chemotherapy was used first in 21% of cases.

A change in stage following laparotomy occurred in 42% of cases (Table 4). The spleen was involved in 36% of cases. Table 5 compares the U.D.H. experience with the Stanford experience. In Puerto Rico 42% had a change in stage, whereas at Stanford 31% changed stage. The complications of surgical staging in our series are shown in Table 6, only 8% of patients developed complications.

A 10% relapse in the abdomen after negative staging laparotomy, was observed in our patients (Table 7). The five-year survival for all cases was 72% (Fig. 1).

For the sake of determining the value of staging laparotomy we have compared the survival in patients with clinical Stage I and Stage II with and without staging

laparotomy. Patients with staging laparotomy had 76% five-year survival, and those without a staging laparotomy had a 67% five-year survival (Fig. 2) ( $p=0.37$ ).

TABLE 1

Age Distribution		
Age	No.	%
1 - 10	20	23
11 - 20	25	28
21 - 30	23	26
31 - 40	10	11
41 - 50	8	9
51 - 60	2	3
	88	

TABLE 2

Site of Initial Manifestation		
Site	No.	%
Upper Neck	52	59
Supraclavicular	15	17
Inguinal	7	8
Mediastinum	3	3
Axillae	5	6
Other	6	7
	88	

TABLE 3

Histology		
	No.	%
Lymph Predominance	12	14
Nodular Sclerosis	28	32
Mixed Cellularity	34	38
Lymph Depletion	5	6
Other	9	10
	88	



TABLE 4

Change in Stage			
Clinical Stage	Surgical Stage	No.	%
I	II	5	
I	III	14	38
I	IV	1	
II	III	12	32
II	IV	4	
III	IV	1	
Changed		37	42
Not Changed		50	57
No Information		1	1

TABLE 5

	Stanford*	U.D.H.
Changed in Stage	31%	42%
Positive Spleen	38%	36%
Positive Liver	5.2%	6.8%
Bone Marrow	2.8%	0

\* Kaplan, H., et al: Hodgkin's Disease Cambridge, Mass. Harvard University Press 2nd Ed. 1980.

TABLE 6

Complications of Surgical Staging		
	No.	%
Infected Wound	6	7
Subphrenic Abscess	1	1
Operative Mortality	0	

Note: A 7 yr. old girl died of meningitis clinically free of Hodgkin's disease, 3 years after staging laparotomy.

TABLE 7

Relapses After Negative Staging Laparotomy		
Site of Relapse	No.	%
Abdomen	4	8
Inguinal	1	2
		10

FIGURE 1

## SURVIVAL ALL STAGES

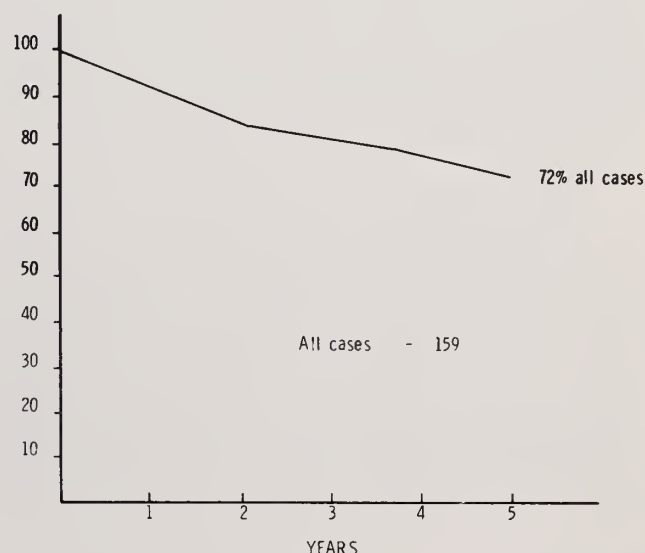
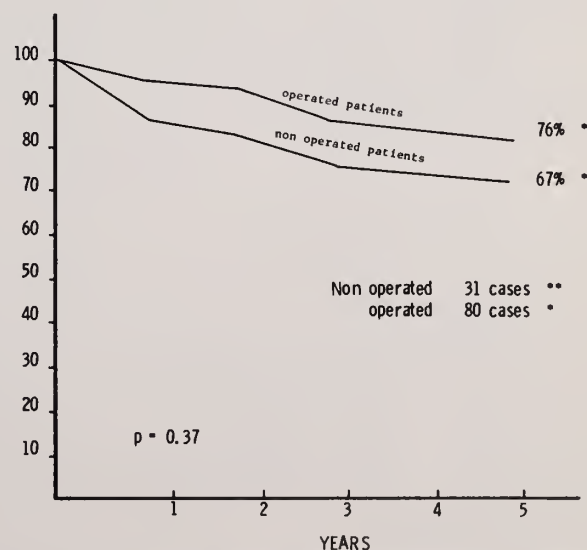


FIGURE 2

## COMPARISON OF CLINICAL STAGE I AND II AND SURGICAL STAGE I AND II PRIOR TO LAPAROTOMY



## Discussion and Conclusions

Staging laparotomy for Hodgkin's Disease has been considered an important tool in discovering subclinical subdiaphragmatic disease. The Stanford series had 31% change in stage, whereas our series had a 42% change in stage. This may be a reflection on the difference in utilization of non-invasive diagnostic procedures (gallium scan, lymphangio-

gram, sonography, computerized tomography, etc.) prior to laparotomy, in the two institutions.

When we compare the five-year survival of clinical Stage I and II patients submitted to surgical staging, with the non operated clinical Stages I and II group, the results would suggest that there is no survival benefit associated with laparotomy (Fig. 2) ( $p=0.37$ ). At first sight it would appear, that patients with clinical Stage I and II submitted to laparotomy staging do better; however these survival curves do not consider age, histology and symptoms associated with "B" status such as fever, and weight loss, all associated with a poor prognosis.

In the group staged with laparotomy the median age was 18 years, as compared with the median age of 32 years in the group without laparotomy. We also found that only 15% of the explored group were substage "B" in comparison with 29% of the group with no laparotomy (Table 8). The B symptoms were associated with a change in stage in 8/12 (67%) of the patients, versus 23/68 (34%) in the group without symptoms. Moreover, the majority (58%), of the group with staging laparotomy were clinical stage I before the procedure versus the group without laparotomy only 19% were Stage I (Table 8). The histologic distribution was similar in the two groups.

infected wounds and 1% subphrenic abscess; there was no operative mortality within 30 days in the 88 cases done at University District Hospital. We had a late death due to meningitis in a 7 year old girl (Table 6). The association of meningitis and splenectomy in children below 10 years old has been previously described.<sup>8</sup>

We as others,<sup>1 4 9 14 15 16 23 28</sup> do not feel that all patients with Hodgkin's disease should have a staging laparotomy, specially in Stages I and II. It is generally agreed that staging laparotomy will change the stage in 30-40% of the patients. This fact has been used to conclude that routine staging laparotomy is of therapeutic value; but clinically occult Stage III disease does not justify laparotomy since such patients can be controlled consistently if they are treated appropriately.<sup>4</sup> Johnson<sup>14 16</sup> has demonstrated that despite a negative staging laparotomy, prophylactic para-aortic irradiation is indicated to prevent abdominal relapses. Radiotherapy limited to anatomical areas above the diaphragm (Mantle) may permit extension of the disease to the abdomen.<sup>14 15</sup> Unsuspected involvement by Hodgkin's disease rarely manifests itself outside of the standard prophylactic fields.<sup>14</sup> In our analysis only 9% (7/80) of the explored group Stage I and II showed disease outside of the standard prophylactic fields at the time of exploration; of these 5.7% (4/7) had B symptoms. If instead

TABLE 8

Patient Characteristics in Operated Versus Non-Operated Clinical Stage I and II				
	Submitted to Surgical Staging		Not Submitted to Surgical Staging	
B Symptoms	12/80	(15%)	9/31	(29%)
Stage Distribution				
Stage I	46/80	(58%)	6/31	(19%)
Stage II	34/80	(42%)	25/31	(81%)
Age Distribution				
Age below 40	73/80	(91%)	20/31	(65%)
Age over 40	7/80	( 9%)	11/31	(35%)
Median	18 years		32 years	
Histological Distribution				
Lymphocytic Predominance	13%		9%	
Nodular Sclerosis	29%		26%	
Mixed Cellularity	43%		56%	
Lymphocytic Depletion	6%		3%	
Other	9%		6%	

The disease free survival for the clinical Stage I and II with laparotomy was 49% in comparison to 36% of the Stages I and II without laparotomy ( $p=0.19$ ).

Most of the cases in this series (58%) had no change in stage (Table 4) after surgery therefore, staging laparotomy added nothing to their management. The complications of surgical staging in Puerto Rico are acceptable, with 7%

of laparotomy, patients with Stages I and II are routinely irradiated to fields including upper abdomen and spleen (extended field), most of the unsuspected intraabdominal disease will be covered; surgical exploration of the abdomen and splenectomy are not required routinely for effective therapeutic management in Hodgkin's disease.<sup>4 14 15 16</sup> Cox<sup>4</sup> found that surgically staged patients not only fail to do better



than those with clinical staging but also there is nothing to suggest that less extensive irradiation, will be used once an exploratory laparotomy has been performed. Abrahamsen<sup>1</sup> showed that staging laparotomy in clinical Stage I and II does not convincingly improve the survival.

We found 10% (5/50) relapses below the diaphragm despite a negative staging laparotomy; three of these patients (3/4) did not receive prophylactic irradiation to para-aortic area. In these patients random biopsies were unreliable in detecting microscopic disease below the diaphragm, with subsequent relapse in these nodes.

At this moment it appears that surgical staging represents a method of selecting a sample of patients with early and favorable disease. Staging laparotomy should be performed in selected cases where a change in stage would alter therapy. The procedure should be done by an experienced surgeon and should include: splenectomy; liver wedge and needle biopsies of both lobes; and biopsy of splenic, para-aortic, iliac and coeliac nodes, even if not enlarged.<sup>2 5 10</sup>

Our analysis does not show any benefit to exploratory laparotomy for Stage IA - IIA Hodgkin's disease. We do not recommend it for this group of patients if radiotherapy will involve the para-aortic and splenic areas as standard treatment. Lymphangiography, computerized tomography or sonography of the abdomen, gallium scan, and liver and spleen scan should be part of the work-up of these patients; the exploration should be limited to Stage IA and IIA with equivocal findings. Stage IB, IIB, and IIIA should be explored because they have high risk of unsuspected liver or lymph node involvement outside of the standard radiotherapy field.

### Acknowledgements

The authors thank Ms. Raquel Torres for the statistical analysis and Ms. Yolanda Vázquez for typing the manuscript.

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# Intravenous vs. Intramuscular Magnesium Sulfate for Preeclampsia

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**Summary:** A total of 38 patients with a diagnosis of severe preeclampsia admitted to the Department of Obstetrics and Gynecology, San Juan City Hospital were treated either with intravenous (n=26) or intramuscular magnesium sulfate (n=12). These patients were followed prospectively. In both groups therapeutic levels were reached and maintained without difficulty. No statistical significant differences in mean serum magnesium levels were found between groups. In our limited series, both methods were found to be safe and simple to manage. The IV method is preferred to avoid the painful injections and allow individual titration.

Pregnancy induced hypertension (PIH) is defined as the occurrence of acute hypertension after the twentieth week of gestation associated with edema and/or proteinuria.<sup>1</sup> This condition has a wide spectrum, ranging from mild to the most severe forms where maternal mortality rate ranges from 0% to 13% and fetal mortality rate as high as 37%.<sup>2</sup> Multi-organ system involvement is common with development of cerebral edema, seizures, pulmonary edema, severe liver disease, disseminated intravascular coagulation and renal dysfunction.<sup>3</sup> Recent reports describe an organism found in patients with PIH as well as gestational trophoblastic disease.<sup>4</sup> These forms are referred as *Hydatosi lualba*. Confirmation by other investigators is required but, if true, definite therapy might be related to antibiotics or immunotherapy. At present, therapy is directed toward preventing convulsions, controlling blood pressure and delivery if the fetus is mature, or if there is evidence of intrauterine growth retardation, fetal jeopardy, worsening PIH or eclampsia. This paper will describe a prospective trial of continuous intravenous (IV) magnesium sulfate ( $MgSO_4$ ) versus intramuscular (IM)  $MgSO_4$  in laboring preeclamptics.

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## Materials and Methods

Twelve patients admitted to the Department of Obstetrics and Gynecology, San Juan City Hospital, with the diagnosis of severe preeclampsia were treated with IM  $MgSO_4$  using the guidelines of Pritchard, et al (see Table I).<sup>5</sup> Specifically a loading dose of 10 gm of  $MgSO_4$  is administered as a 50% solution in divided doses, one half of the dose deep IM in the upper outer quadrant of each buttock. A maintenance dose of 5 gm of 50% magnesium sulfate is administered every 4 hours.

TABLE I

Use of Intramuscular Magnesium Sulfate	
A.	10 gm loading dose, one half of the dose deep IM in the upper outer quadrant of each buttock.
B.	A 5 gm maintenance dose (deep IM) every 4 hours. <ol style="list-style-type: none"> <li>1. If patellar reflexes are present</li> <li>2. There is no respiratory depression, and</li> <li>3. Urine output is greater than 100 ml./4 hours</li> </ol>
C.	Urine output every 4 hours
D.	Vital signs with blood pressure every 1 to 4 hours.

Twenty-six severe preeclamptic patients received intravenous  $MgSO_4$  therapy. All patients received an IV bolus of 4 gm  $MgSO_4$ , then continuous infusion was continued at a rate of 1.5 to 2.5 gm/hr. This infusion was increased or decreased according to symptomatology (central nervous system irritability) and urine output. The rate of infusion was increased if symptomatology worsened, or decreased if urine output dropped (see Table II). The groups were similar in age, parity, race and socioeconomic status.

TABLE II

Use of Intravenous Magnesium Sulfate	
A.	4 gm IV bolus
B.	Continuous IV infusion at a rate of 1.5 to 2.5 gm/hours depending on: <ol style="list-style-type: none"> <li>1. If patellar reflexes are present</li> <li>2. There is no respiratory depression</li> <li>3. Urine output is greater than 100 ml./4 hours</li> </ol>
C.	Urine output every 4 hours
D.	Vital signs with blood pressure every 1 to 4 hours.



## Results

The IM  $\text{MgSO}_4$  group had a mean serum magnesium concentration of  $5.05 \pm 1.0 \text{ mg\%}$  at 1 1/2 hours after IM injection was given, and similar levels were maintained throughout labor. The IV  $\text{MgSO}_4$  group had mean serum magnesium levels of  $5.3 \pm 0.8 \text{ mg\%}$  at 1 to 1 1/2 hours after infusions were started. Even though our numbers are small and we are cognizant of the fact that a larger series is needed for a definite statistical analysis, no statistically significant difference was found between groups (paired T test). By increasing the infusion on those patients with levels below 4  $\text{mg\%}$ , the mean serum magnesium levels rose gradually to therapeutic levels. Both methods were found to be safe and simple to manage. In this series we did not have eclampsia in any of our patients.

## Comment

The use of  $\text{MgSO}_4$  as prophylaxis against seizures has proven itself over a long period of time. Some of the benefits of using  $\text{MgSO}_4$  are that it definitely controls or prevents eclampsia, the patient is alert and awake and not heavily sedated as when barbiturates, tranquilizers, or narcotics are used, airway problems and aspiration of stomach contents are less likely, the fetus is not further jeopardized by anti-convulsants, and  $\text{MgSO}_4$  is easily managed by physician and nurses.<sup>3</sup> However, it is necessary that a physician or trained nursing personnel always be in attendance so that overdoses can be prevented. Toxic doses depress the central nervous system, and signs of toxicity are reached at 10  $\text{mg\%}$  at which point patellar reflex is lost. Respiratory arrest occurs at 15  $\text{mg\%}$  and total body paralysis at approximately 25  $\text{mg\%}$ . Therapeutic anticonvulsant levels are achieved when concentrations of magnesium reach 4 to 7.5  $\text{mg\%}$ . Magnesium sulfate is almost exclusively cleared from the circulation by the kidneys. It is very important to follow urine output in order to avoid toxic overdoses. The drug must not be given in the absence of patellar reflexes.

In our limited series, both methods were found to be safe and simple to manage. The IV method is preferred to avoid the painful injections and allow individual titration of therapy. Both groups were seizure free during treatments attesting to the maintenance of therapeutic levels on both groups. Differences in the mean serum magnesium levels between groups were not statistically significant.

With close surveillance of the patient by well trained physicians or nursing personnel, magnesium sulfate either in IV or IM route is a safe prophylactic anticonvulsant therapy in cases of PIH.

## Resumen

Un total de treinta y ocho pacientes con diagnóstico de preeclampsia severa fueron admitidas al Departamento de Obstetricia y Gynecología, Hospital Municipal de San Juan. Estas pacientes fueron tratadas de manera prospectiva con sulfato de magnesio por vía intravenosa ( $n=26$ ) o intramuscular ( $n=12$ ). En ambos grupos niveles terapéuticos fueron alcanzados y mantenidos sin dificultad. La diferencia en niveles de magnesio entre los dos grupos estudiados no fue

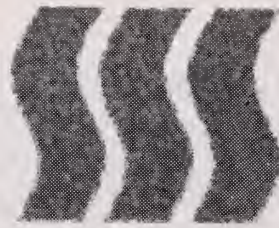
estadísticamente significativa. Ambos métodos, endovenoso o intramuscular, son simples y seguros. El método endovenoso es preferido ya que permite un mejor ajuste de la dosis necesaria, y evita múltiples inyecciones dolorosas.

## Acknowledgements

We want to thank Drs. Luis Vázquez, Fernando Castro, Francisco Pla, Angel Monserrate and the nursing staff of the San Juan City Hospital for their help in the clinical management of these patients.

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# Foro de Medicina Nuclear

## Coronary and Valvular Heart Disease: Gated Cardiac Blood Pool Study

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Julio V. Rivera, M.D.

### Case Summary

A 58 year old male with history of insulin dependent diabetes mellitus was referred for cardiac functional evaluation. He was asymptomatic until February 1978 when he experienced an anterolateral wall myocardial infarct which was accompanied by mild congestive heart failure. Systolic and diastolic aortic murmurs were detected at that time.

Two months after this episode he again suffered a severe episode of chest pain and was treated for unstable angina.

After discharge the patient continued to experience progressive angina and dyspnea on exertion. He was followed in a private cardiology center. He has been on a regimen of digoxin, furosemide, spironolactone, isosorbide dinitrate and procainamide hydrochloride.

On physical examination the patient was found not in distress. The lungs were clear to auscultation. A grade 2/VI systolic ejection murmur and a diastolic aortic murmur grade 1/VI were heard. A dyskinetic area on apex and a S3 gallop were found.

The chest x-ray revealed cardiomegaly. The electrocardiogram showed old anterolateral wall and inferior wall

myocardial infarcts. An echocardiogram revealed significant left ventricular dilatation and aortic insufficiency.

A gated cardiac blood pool study ( $^{99m}\text{Tc}$  RBC) performed on April 15 1982 provided evidence of left ventricular dilatation, left ventricular ejection fraction of 34% and a large focal region of altered wall motion involving portions of the anterior, lateral, and inferior walls. (Figure 1) A left to right stroke volume ratio of 1.36 provided evidence of mild aortic valve insufficiency.



Figure 1. Functional image derived from serial images of the cardiac cycle, left anterior oblique view ( $^{99m}\text{Tc}$  RBC). Darkest shades indicate greatest motion, lighter ones represent reduced motion. A large region of impaired motion involves the region about the cardiac apex (MI). LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium.

## Discussion

Multiple gated acquisition is the method most commonly employed for the performance of radionuclide ventriculography. In this approach Technetium 99m labeled red blood cells are administered and allowed to come to equilibrium in the vascular compartment. It is possible to record gated blood pool images from various projections. Data from several hundred beats is collected to form an average or composite several hundred beats is collected to form an average or composite cardiac cycle. Data acquisition is synchronized with the electrocardiogram. Images are taken in two projections, anterior and left anterior oblique, which together show most of the segments of the left ventricle.<sup>1</sup>

Quantitative studies supplement the subjective interpretation of the images. Abnormalities may be found in regional wall motion, ventricular time activity curves, ejection fraction, right to left ventricular stroke count ratios and ventricular volumes at different stages of the cardiac cycle.

Measurement of left ventricular function by radionuclide ventriculography is helpful in predicting morbidity and mortality in patients with acute myocardial infarction.<sup>2</sup> In patients with coronary artery disease, but no evidence of transmural infarction, global ventricular function is frequently normal at rest. In these patients exercise may uncover left ventricular dysfunction.<sup>3</sup>

In patients with myocardial infarction or severe coronary stenosis gated blood pool studies at rest may show all grades of wall motion abnormality, from hypokinesia to akinesia and frank aneurysm formation. Follow-up studies on patients with acute myocardial infarction have been suggested for determining the presence of residual ischemic segments at risk.

For evaluation of a patient with left heart failure from known or suspected coronary artery disease, a gated blood pool study may be performed. Patients with poor global function and an ejection fraction of less than 30 percent are known to have a high surgical mortality rate. Patients who are shown to have moderately sized areas of akinesia or dyskinesia associated with relatively well preserved motion in the remainder of the ventricle make the most likely surgical candidates.<sup>1</sup>

Patients with valvular heart disease may have heart failure on the basis of mechanical factors as in volume overloading in aortic insufficiency or depression of ventricular contractile function secondary to coronary artery disease. Significant coronary disease is found in about 20% of patients with valvular disease aged 40 or more years.<sup>4</sup> Radionuclide angiography can define the impact of the valvular abnormality on cardiac chamber size and function and the role of coronary artery disease suspected on the basis of regional left ventricular wall motion abnormalities. The severity of mitral or aortic regurgitation can be assessed from stroke (left ventricular/right ventricular) volume ratios. In the absence of valve regurgitation, the stroke volume of the right ventricle is equal to that of the left. For patients with regurgitation, the stroke volume of the left ventricle is greater than that of the right.<sup>5</sup> In valvular heart disease there are chronic compensatory mechanisms, such as dilatation and hypertrophy which tend to maintain the ejection fraction in the normal range. To uncover compensated and diminished reserve function, ejection fraction should be determined with stress as well as at rest.<sup>5</sup> Failure of the ejection fraction to increase significantly

with stress may prove to be the earliest sign of deteriorating left ventricular function, and so the timing of surgical intervention may be optimized.

The ability to follow both global and regional changes in biventricular function in response to therapeutic or diagnostic interventions is unique to radionuclide ventriculography among currently available cardiac imaging modalities.

In this patient the radionuclide study provided objective quantitative evaluation of each component of the patient's heart disease. Myocardial disease due to coronary artery occlusion was shown to be the most important pathophysiological element.

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




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The effectiveness of diazepam in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindications:** Tablets or capsules in children under 6 months of age; known hypersensitivity; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** As with most CNS-acting drugs, caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of predisposition to habituation/dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because their use is rarely a matter of urgency and because of increased risk of congenital malformations, as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**ORAL.** Advise patients against simultaneous ingestion of alcohol and other CNS depressants.

Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral forms adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may be associated with temporary increase in frequency and/or severity of seizures.

**INJECTABLE.** *To reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling and, rarely, vascular impairment when used I.V.: inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer Injectable Valium directly I.V., it may be injected slowly through the infusion tubing as close as possible to the vein insertion.*

Administer with extreme care to elderly, very ill, those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; concomitant use of barbiturates, alcohol or other CNS depressants increases depression with increased risk of apnea; have resuscitative facilities available. When used with narcotic analgesic eliminate or reduce narcotic dosage at least 1/3; administer in small increments. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs.

Has precipitated tonic status epilepticus in patients treated for petit mal status or petit mal variant status. Not recommended for OB use.

Efficacy/safety not established in neonates (age 30 days or less); prolonged CNS depression observed. In children, give slowly (up to 0.25 mg/kg over 3 minutes) to avoid apnea or prolonged somnolence; can be repeated after 15 to 30 minutes. If no relief after third administration, appropriate adjunctive therapy is recommended.

**Precautions:** If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of diazepam, i.e., phenothiazines, narcotics, barbiturates, MAO inhibitors and antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or over-sedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed and tolerated).

The clearance of diazepam and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

**INJECTABLE.** Although promptly controlled, seizures may return; readminister if necessary; not recommended for long-term maintenance therapy. Laryngospasm/increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic, have necessary countermeasures available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly/debilitated.

**Adverse Reactions:** Side effects most commonly reported were drowsiness, fatigue, ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity,

insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, discontinue drug.

Because of isolated reports of neutropenia and jaundice, periodic blood counts, liver function tests advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, observed in patients during and after diazepam therapy are of no known significance.

**INJECTABLE.** Venous thrombosis/phlebitis at injection site, hypoaactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia. In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm/pain in throat or chest have been reported.

**Dosage:** Individualize for maximum beneficial effect.

**ORAL. Adults:** Anxiety disorders, relief of symptoms of anxiety—Valium (diazepam/Roche) tablets, 2 to 10 mg b.i.d. to q.i.d.; or 1 or 2 Valrelease capsules (15 to 30 mg) daily. Acute alcohol withdrawal—tablets, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; or 2 capsules (30 mg) the first 24 hours, then 1 capsule (15 mg) daily as needed. Adjunctively in skeletal muscle spasm—tablets, 2 to 10 mg t.i.d. or q.i.d.; or 1 or 2 capsules (15 to 30 mg) once daily. Adjunctively in convulsive disorders—tablets, 2 to 10 mg b.i.d. to q.i.d.; or 1 or 2 capsules (15 to 30 mg) once daily.

**Geriatric or debilitated patients:** Tablets—2 to 2½ mg 1 or 2 times daily initially, increasing as needed and tolerated (see Precautions). Capsules—1 capsule (15 mg) daily when 5 mg oral Valium has been determined as the optimal daily dose.

**Children:** Tablets—1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use in children under 6 months). Capsules—1 capsule (15 mg) daily when 5 mg oral Valium has been determined as the optimal daily dose (not for use in children under 6 months).

**INJECTABLE:** Usual initial dose in older children and adults is 2 to 20 mg I.M. or I.V., depending on indication and severity. Larger doses may be required in some conditions (tetanus). In acute conditions injection may be repeated within 1 hour, although interval of 3 to 4 hours is usually satisfactory. Lower doses (usually 2 to 5 mg) with slow dosage increase for elderly or debilitated patients and when sedative drugs are added. (See Warnings and Adverse Reactions.) For dosages in infants and children see below; have resuscitative facilities available.

**I.M. use:** by deep injection into the muscle.

**I.V. use:** inject slowly; take at least one minute for each 5 mg (1 ml) given. Do not use small veins, i.e., dorsum of hand or wrist. Use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute Valium with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer Valium directly I.V., it may be injected slowly through the infusion tubing as close as possible to the vein insertion.

Moderate anxiety disorders and symptoms of anxiety, 2 to 5 mg I.M. or I.V., and severe anxiety disorders and symptoms of anxiety, 5 to 10 mg I.M. or I.V., repeat in 3 to 4 hours if necessary; acute alcohol withdrawal, 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary. Muscle spasm, in adults, 5 to 10 mg I.M. or I.V. initially, then 5 to 10 mg in 3 to 4 hours if necessary (tetanus may require larger doses); in children administer I.V. slowly; for tetanus in infants over 30 days of age, 1 to 2 mg I.M. or I.V., repeat every 3 to 4 hours if necessary; in children 5 years or older, 5 to 10 mg repeated every 3 to 4 hours as needed. Respiratory assistance should be available.

Status epilepticus, severe recurrent convulsive seizures (I.V. route preferred), 5 to 10 mg adult dose administered slowly, repeat at 10- to 15-minute intervals up to 30 mg maximum. Repeat in 2 to 4 hours if necessary, keeping in mind possibility of residual active metabolites. Use caution in presence of chronic lung disease or unstable cardiovascular status. Infants (over 30 days) and children (under 5 years), 0.2 to 0.5 mg slowly every 2 to 5 min., up to 5 mg (I.V. preferred). Children 5 years plus, 1 mg every 2 to 5 min., up to 10 mg (slow I.V. preferred); repeat in 2 to 4 hours if needed. EEG monitoring may be helpful.

In endoscopic procedures, titrate I.V. dosage to desired sedative response, generally 10 mg or less but up to 20 mg (if narcotics are omitted) immediately prior to procedure; if I.V. cannot be used, 5 to 10 mg I.M. approximately 30 minutes prior to procedure. As preoperative medication, 10 mg I.M.; in cardioversion, 5 to 15 mg I.V. within 5 to 10 minutes prior to procedure. Once acute symptomatology has been properly controlled with injectable form, patient may be placed on oral form if further treatment is required.

**Management of Overdosage:** Manifestations include somnolence, confusion, coma, diminished reflexes. Monitor respiration, pulse, blood pressure; employ general supportive measures, I.V. fluids, adequate airway. Use levarterenol or metaraminol for hypotension. Dialysis is of limited value.

**How Supplied:**

**ORAL.** Valium scored tablets—2 mg, white; 5 mg, yellow; 10 mg, blue—bottles of 100 and 500; Prescription Paks of 50, available in trays of 10; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25 and in boxes containing 10 strips of 10.

Valrelease (diazepam/Roche) slow-release capsules—15 mg (yellow and blue), bottles of 100; Prescription Paks of 30.

**INJECTABLE.** Ampuls, 2 ml, boxes of 10; Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.





# Temas de Especialidades Pediátricas

## Diagnóstico y Tratamiento de la Diabetes Infantil (Parte II)

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### Tratamiento

El tratamiento adecuado de la diabetes sacarina se fundamenta en cuatro pilares: Educación, Dieta, Insulina, y Ejercicio (EDIE). Los objetivos del tratamiento incluyen:

TABLA V

Objetivos del Tratamiento
1. Ajuste emocional adecuado
2. Crecimiento y desarrollo normal
3. Ausencia de síntomas
4. Glicosuria menor 10% de ingesta de glucosa
5. Ausencia de reacciones hipoglicémicas
6. Ausencia de enfermedad iatrogénica
7. Conocimiento de la enfermedad y sus complicaciones
8. Ajuste escolar adecuado
9. Actividades normales para sujetos de su edad.

El médico que maneja estos pacientes suele encontrar problemas de ajuste emocional a una enfermedad crónica, a las restricciones dietéticas, la terapia insulínica y control adecuado de las pruebas de sangre y orina.

La descripción del tratamiento puede subdividirse, para fines prácticos, en cuatro apartados: 1) acidosis, 2) etapa postacidótica, 3) establecimiento de normoglicemia, y 4) seguimiento del diabético controlado.

#### 1) Acidosis Diabética

El tratamiento de un niño con acidosis diabética es una emergencia, requiriendo un trabajo de equipo, que funcione a la perfección entre el médico, la enfermera, la nutricionista, el personal de farmacia, la trabajadora social y el laboratorio. El estado de gravedad vendrá determinado por el cuadro clínico

y químico, con interés particular en el grado de suficiencia circulatoria y la atención a la acidosis metabólica. Es fundamental el diagnóstico precoz, por lo que resulta muy útil la determinación rápida de glicemia con glucocintas y refractómetros. Si es necesario se debe cateterizar al paciente para obtener orina para azúcar, acetona y determinación de la excreción total de líquidos.

La terapia inicial estará encaminada a corregir la cetoacidosis, reemplazar el agua y electrolitos intra, y extracelulares, suplir la insulina necesaria, y, cuando esté indicado, el tratamiento de la infección subyacente. En ocasiones, el tratamiento de la insuficiencia circulatoria ocupa el primer lugar, empleándose expansores plasmáticos.

Una vez que se confirma el diagnóstico se comienza una infusión endovenosa, para expandir el volumen circulatorio, que consiste en una solución salina isotónica a una razón de 20 ml./Kg. en los primeros 30 a 60 minutos. Si hay acidosis severa presente (pH 7.15, respiración de Kussmaul,  $\text{CO}_2$  menor de 10 mM/L) se deberá añadir bicarbonato sódico en una dosis de 1 a 2 mEq./kg. de peso corporal. Se puede emplear una solución al 7.5% de bicarbonato que contiene 44.6 mEq. en 50 ml., es decir, aproximadamente 1 mEq. por mililitro. Su administración endovenosa directa conlleva una sobrecarga osmótica que podría dar lugar a deshidratación de células cerebrales. Por ello, se recomienda su dilución con agua destilada. La terapia inicial debe prescindir de glucosa, especialmente si los valores de glicemia son superiores a los 300 mgr. %.

La terapia insulínica es fundamental para corregir el cuadro metabólico. Se deberá emplear la insulina menos antiagénica posible, y en la forma de insulina de acción rápida. La dosificación y horario de la misma variará de acuerdo a la ruta de administración siguiendo el esquema de Alberti para la vía endovenosa, intramuscular o subcutánea.<sup>31</sup> Se utilizarán dosis fisiológicas o microdosis de insulina, con seguimiento adecuado de las glicemias y del cuadro electrolítico e hídrico del paciente.

TABLA VI

Infusión Continua con Dosis Fisiológicas de Insulina
Dosis inicial de 0.1 unidades de insulina rápida/ kg. Infusión continua e/v de 0.1 unid./kg./hr. Niño de 30 Kg.: añadir 25 unid. de insulina rápida a 500 cc. de NS Infundir insulina en vena distinta a la usada para hidratación. Infusión de 60 cc./hr (3 unid./hr.) Cuando la glicemia alcance 300 mgr. %, descontinuar NS y añadir glucosa al 5% y se disminuye la insulina a 0.05 unid. /kg./hr. Puede descontinuarse infusión e/v, y continuar con insulina s/c a dosis de 0.25 a 0.5 unid. por kg. cada 6 a 8 horas.

La cantidad de líquido endovenoso a administrarse en 24 horas dependerá del grado de deshidratación, la cual suele ser severa en los pacientes comatosos. Su corrección habrá de calcularse según la superficie corporal del niño y el grado de deshidratación presente. La deshidratación severa requiere de 3000 a 4000 cc/m<sup>2</sup>/día, la moderada de 2000 a 3000 cc/m<sup>2</sup> día. A los líquidos totales se les habrá de restar la porción inicial de la primera hora.

El paciente se mantendrá en solución salina (Normal Salino 0.45NS según el grado de osmolaridad) hasta que la acidosis y la hiperglicemia se reduzcan a valores cercanos a la normalidad. En ese momento se comenzará la terapia con una solución electrolítica glucosada.

El paciente no debe tomar nada por boca en las primeras 6 horas. Posteriormente, si no vomita, se le darán líquidos por boca que contengan potasio, tal como el jugo de naranja (40 mEq. de potasio y 10% de carbohidratos).

No se administrará potasio hasta que el paciente comience a orinar. En la terapia inicial no suele añadirse; utilizándose, cuando es necesario, a las 4 a 6 horas de comenzada la terapia, sino hay contraindicación. Se emplea cloruro o fosfato potásico diluido en el suero (no en forma de bolo endovenoso) en una dosis de 20 a 40 mEq./L.

Los pacientes que presenten coma diabético hiperosmolar no-cetósico han de recibir su terapia inicial con una solución salina a una concentración 1/2 Normal. La terapia insulínica deberá ser cuidadosa debido a su extrema sensibilidad a ella.

La utilización de sistemas de infusión continua y programada, bien los sistemas abiertos, o bien los sistemas cerrados, favorecen una más rápida recuperación y control de los pacientes.

## 2) Estado Post-Acidósico

El paciente se ha de mantener en insulina de acción rápida por lo menos dos días, para así determinar sus requerimientos diarios de la misma. Estos podrían determinarse, si se cuenta con las facilidades, con el empleo del páncreas artificial.

Inicialmente se debe comenzar con una dieta líquida o blanda y según la vaya tolerando, se modificará a una dieta de consistencia normal. El paciente ingerirá tres comidas y dos a tres meriendas dependiendo del tratamiento insulínico que reciba. La insulina rápida deberá administrarse con las comidas, dando dosis suplementarias, si necesarias, en la madrugada.

## 3) Establecimiento de la Normoglicemia

Una vez se conocen los requisitos diarios de insulina, el paciente se ha de cambiar a una insulina de acción intermedia del tipo de NPH o LENTE. Un número significativo de pacientes precisan de una combinación de insulina de acción intermedia y rápida, para poder lograr así un perfil de glicemias adecuado, sin excursiones exageradas postprandiales. Ello ocurre con más frecuencia en las primeras horas de la mañana, por lo que la mayor parte de los pacientes que así lo requieren son tratados con una combinación en la mañana.

Un gran número de pacientes, por lo menos al principio de la terapia insulínica, logran un control adecuado de la glicemia con una sola inyección diaria. Mientras no se presente descompensación y dependencia total a la insulina se

justifica el empleo de una dosis única siempre y cuando los niveles de glicemia sean aceptables y los niveles de hemoglobina glicosilada se mantengan en cifras de control.

En nuestro medio, las mezclas de preparados insulínicos han de hacerse al momento debido al elevado contenido de protamina o de zinc, ya que el exceso de estas sustancias convierten la insulina rápida en una de periodo de acción variable obteniéndose una mezcla de duración desconocida y muy variable.

La insulina de acción intermedia se suele comenzar a una dosis que corresponda a 2/3 ó 3/4 partes de los requisitos diarios de la insulina rápida requerida para el control diario. La fracción restante se suele administrar, por mezcla en la jeringuilla, con insulina de acción rápida. Se titula el paciente en los días subsiguientes, añadiendo las cantidades adicionales de insulina, según sea el caso, hasta lograr el control glicémico adecuado. Dependiendo del perfil glicémico y de la duración de la insulina administrada al paciente se utilizarán una o dos inyecciones diarias.

Si se dispone de los medios para obtener sistemas de infusión basal y programada de insulina, éste constituirá el tratamiento ideal al simular de forma más exacta los mecanismos fisiológicos del organismo. Desgraciadamente nuestros sistemas sanitarios y los planes médicos prepagados aún no comprenden esto, no compensando al paciente por estos instrumentos que obviamente a largo plazo abaratarían los costos médicos incurridos.

En los primeros días de terapia se ha de evaluar si los valores de glicemia corresponden a los valores de glucosa en orina, determinando el dintel renal aproximado e individualizado de cada paciente. Ello es importante ya que la determinación de glucosuria resulta un índice relativamente barato para el seguimiento y control diario del paciente en la casa. Como es lógico, aquellos pacientes que puedan costearse el gasto de glucocintas o de refractómetros más exactos estarán más protegidos y mejor controlados al poseer valores de glicemia al minuto.

Los niveles de glicemia aceptables para el control del niño diabético deberán ser superiores a los 100 mg.%, según nuestros criterios, e inferiores a los 200 mg.% en ayunas y, lógico, aquellos pacientes que puedan costearse el gasto de glucocintas o de refractómetros más exactos estarán más protegidos y mejor controlados al poseer valores de glicemia al minuto.

Los niveles de glicemia aceptables para el control del niño diabético deberán ser superiores a los 100 mg.%, según nuestros criterios, e inferiores a los 200 mg.% en ayunas y postprandiales de dos horas en la mañana. De esta forma evitaremos hipoglicemias, mayormente en niños pequeños donde por múltiples razones la alimentación puede variar rápidamente. Con valores a este nivel, tras 15 años de práctica de la especialidad, hemos observado un crecimiento adecuado en los niños, al igual que escasas hospitalizaciones y complicaciones a corto y largo plazo.

Durante los primeros meses posteriores al inicio del tratamiento, se observan con relativa frecuencia remisiones parciales o totales de la condición, requiriendo estos niños menores cantidades de insulina. Es lo que se ha llamado el periodo de "luna de miel" el cual puede ser de duración muy variada, usualmente de dos a tres meses, pero que ha sido observado por nosotros hasta el año y medio de duración. Nuestros datos de 56 pacientes revelan que la misma fue parcial en tres pacientes, con disminución en más de una tercera parte de los requeri-



mientos insulínicos, y total en otros trece pacientes. Estos últimos se mantuvieron en dosis mínimas de una a dos unidades diarias de insulina (salvo los que presentaban intolerancia a los carbohidratos que respondieron a tratamiento dietético). Se observó remisión total en cuatro diabéticos tipo 1, dos con Intolerancia a los Carbohidratos y en seis pacientes con Diabetes tipo 2 o Intolerancia a los Carbohidratos reclasificados como Anomalia Previa de Tolerancia a Glucosa. Dos pacientes tuvieron anomalías del perfil glicémico con hiperglicemia e hipoglicemia sintomática. Del tratamiento agresivo inicial y del empleo de insulinas lo menos antigénicas posibles dependerá la inducción de este periodo de luna de miel.

Los niños tratados con insulina de acción intermedia precisan de tres comidas y dos meriendas, siguiendo el periodo de acción de esta insulina administramos meriendas de 2 a 3 P.M. y antes de acostarse a las 9 P.M. En los que reciben una mezcla de insulina de acción intermedia con insulina rápida en la mañana, y en los que están en dos dosis diarias (en la mañana con el desayuno y en la noche con la cena) añadimos una tercera merienda a las dos horas de administrada la insulina de la mañana, con el fin de evitar hipoglicemias a estas horas.

A la hora de preparar una mezcla insulínica hemos de tener sumo cuidado con la misma para así no alterar los preparados insulínicos. Así, en el caso de insulina NPH, que es la empleada por nosotros, y la de acción rápida, procedemos de la siguiente forma:

1. Utilizar jeringuilla esterilizada (hervida o desechable)
2. Conocer bien la dosis de cada una de las insulinas
3. Inyectar en el frasco de preparado turbio (acción intermedia) una cantidad de aire igual al volumen de la dosis que se va a extraer. Sacar la aguja sin aspirar la dosis.
4. Inyectar en el frasco de insulina no modificada (acción rápida, transparente) un volumen de aire igual al de la dosis que se va a extraer del frasco.
5. Invertir el frasco de insulina de acción rápida con la aguja introducida al mismo, y aspirar la dosis deseada.
6. Introducir nuevamente la aguja en el frasco de insulina turbia (de acción intermedia) y extraer la cantidad requerida.

La insulina se mezclará por sí sola en la jeringuilla, por lo que no hay que agitar la misma.

Una buena técnica de inyección es fundamental para reducir a un mínimo las reacciones locales a corto y a largo plazo. La misma deberá ser aséptica, con las jeringuillas y las agujas adecuadas. No se debe permitir el empleo de otro tipo de jeringuillas que no sean para insulina y a la concentración específica del preparado que se esta utilizando.

El lugar de inyección se debe de variar cada día, administrando la misma en el brazo, muslo, nalgas, y de preferencia en el abdomen. El paciente deberá de tener un programa del lugar de inyección previsto para cada día y semana.

Los requerimientos de insulina varían con cada paciente estando relacionados con la etapa de evolución de su enfermedad. En nuestra casuística hemos observado:

TABLA VII

Requerimiento Total de Insulina - Unidades			
	Total	Convencional	Purificada
Todos	44.57 N 47	46.69 N 34	39 N 13
Hembras	47.75 N 20	50.287 N 14	41.83 N 6
Varones	42.22 N 27	42.09 N 21	36.57 N 7

El 72% de nuestros pacientes emplean insulina convencional no purificada debido al costo más elevado de esta última. Tanto en los varones como en las hembras, el empleo de insulinas purificadas resulta en un menor gasto de unidades totales de insulina. Cabe añadir que nuestros pacientes en tratamiento con insulinas purificadas eran los peor controlados por lo que pudo convencerse a los padres del gasto adicional, lo que implica que de usarse en todos los pacientes la diferencia en cifras sería aún mayor.

Al evaluar los requerimientos insulínicos por kilogramo de peso corporal observamos:

TABLA VIII

Insulina - Unidades por kilogramo de Peso			
	Todos	Conv./Kg.	Pp./Kg.
Todos	.9004 N 47	.9579 N 34	.7499 N 13
Hembras	1.068 N 20	1.529 N 14	.8937 N 6
Varones	.7697 N 27	.81975 N 20	.6217 N 7

Se confirma el menor requerimiento insulínico al emplearse las insulinas purificadas monoespecie.

Al analizar estadísticamente los requerimientos insulínicos por peso, encontramos los siguientes datos:

TABLA IX

Unidades de Insulina por Kg. de Peso			
	Todos N 34	Varones N 20	Hembras N 14
Mínimo	0.25	0.25	0.765
Máximo	2.5	1.44	2.5
"Range"	2.25	1.19	1.735
Promedio	0.9579	0.8198	1.553
Mediana	0.8365	0.7855	1.07
"Mid-Range"	1.375	0.845	1.633
Desv. Estand.	0.38522	0.24791	0.46428
Varianza	0.148396	0.061459	0.215552

Observamos una gran variabilidad de individuo a individuo con el rango o "range" de 2.25 unidades, al igual que en los demás parámetros incluidos.

Dos terceras partes de nuestros pacientes insulínoddependientes están en dos dosis de insulina diaria, observándose la frecuencia de dosis en los mismos en la siguiente tabla:

TABLA X

No. Dosis	Insulina - Número de Dosis			
	Total Pctes.	D.I.D.	Hembras	Varones
0	10/57 17.54%	———	3/20 15%	7/27 25.9%
1	16/57 28.07%	16/47 34.04%	9/20 45%	7/27 25.9%
2	31/57 54.39%	31/47 65.96%	11/20 55%	20/27 74%

De los diez pacientes no-insulínoddependientes uno de ellos requirió la misma por espacio de dos años en cantidades superiores a las 50 unidades diarias, al presentar franco sobrepeso. Al presente se encuentra en un peso ideal, manteniendo niveles de glicemia normales sin requerir medicamento alguno.

El 89% de los pacientes insulínoddependientes estudiados (42/47) recibieron terapia on mezcla de insulina de acción rápida e intermedia en la mañana. Un paciente recibió además una mezcla similar con la dosis de la tarde. Observamos en ellos una gran variabilidad como detalla el siguiente análisis estadístico:

TABLA XI

Mezcla Insulina Rápida - Intermedia	
Mínimo	0.05
Máximo	0.5
"Range"	0.45
Promedio	0.310762
Mediana	0.3415
"Mid-Range"	0.275
Desv. Estandard	0.137418
Varianza	0.0188837

Se observa una gran variabilidad en el rango y la proporción de máximo a mínimo. Ello nos obliga a individualizar cada paciente para su dosis de mezcla y no justifica el empleo libre de premezclas estables en todos los pacientes. Dichas mezclas serán útiles para aquellos pacientes que requieran la proporción establecida por la misma. En algunos pacientes mediante el empleo de meriendas adecuadas podrían utilizarse las mezclas después de una estandarización de su terapia medicamentosa y dietética, la cual, recalamos, ha de ser individualizada y no sujeta a patrones específicos.

### Dieta

Junto con la educación diabetológica la dieta constituye el aspecto más importante en el tratamiento de todo diabético. En el caso de los niños la asesoría dietética deberá abarcar a todas las personas envueltas en su cuidado y manejo, a la vez

que se les instruye deberá hacerles ver el valor terapéutico de la misma. No nos podemos conformar con que uno de los padres, o la pareja tan sólo se hagan responsables de la misma, ya que con frecuencia los abuelos, otros familiares inmediatos, el personal escolar y otros, cometen errores por ignorancia o por falta de información.

Los maestros deberán tener conocimiento del horario de las comidas y las meriendas, del niño, a la vez que conocer la importancia de que se cumpla con las mismas. Bajo ninguna circunstancia deberán prohibirle al niño el que las lleve a cabo a las horas que le corresponda. Si el niño come en el comedor escolar, habrá de estar informado el personal del mismo para el debido ajuste a sus comidas.

El seguimiento del horario estricto de las comidas y las meriendas deberá ser recalado a los familiares del niño. Las crisis de hipoglicemia en los domingos en la mañana y en los días de fiesta, por atraso del desayuno, podrían resultar fatales al mismo. Hemos de recordar que se es diabético veinticuatro horas al día, y que la enfermedad no cuenta con los días de fiesta y las vacaciones, la misma NO LE DA VACACIONES AL PACIENTE.

La dieta del niño diabético habrá de ajustarse según su edad y estado nutricional. El contenido calórico de la misma se calculará a base de 1,000 calorías más 100 calorías por año de edad. En la pubertad se dará un suplemento de 150 a 200 calorías más. En los obesos se reducirá el total de calorías y en los delgados se podrá dar una cantidad extra. Además del total de calorías se tratará de dar una dieta alta en fibra y baja en grasas.

El paciente ingerirá tres comidas y de dos a tres meriendas, dependiendo del tratamiento insulínico que reciba. Aquellos con una sola dosis de insulina de acción intermedia podrán emplear dos meriendas, una a media tarde y otra antes de irse a la cama siempre y cuando no presente hipoglicemia a media mañana. Estos últimos, al igual que aquellos que utilicen dos inyecciones de insulina diaria, o que empleen una mezcla de insulina rápida e intermedia en la mañana, requerirán otra merienda a las dos horas de administrada la insulina.

Se debe hacer hincapié en el concepto de que no se trata de una dieta o restricción marcada de alimentos, sino más bien de un PROGRAMA NUTRICIONAL adecuado para el crecimiento del niño donde podrá ingerir la mayor parte de los alimentos que consume la familia en cantidades limitadas, pero suficientes. Los familiares y el niño, cuando sea posible, deberán conocer a cabalidad las listas de alimentos equivalentes y sus cantidades. Logrado esto no será problema alguno el que la puedan llevar a cabo.

El uso de edulcorantes no está contraindicado y se debe estimular su uso. De preferencia se utilizarán aquellos productos naturales, tipo lactosa, de bajo contenido calórico.

Es fundamental en los niños el seguimiento de una dieta adecuada, para lograr un buen control, evitar hipoglicemias, y conseguir un crecimiento normal.

### Ejercicio

El niño diabético puede y debe realizar las mismas actividades que sus compañeros y amigos. Podrá practicar cualquier tipo de deportes siempre que se prevea el consumo adecuado de alimentos y a las horas específicas. Cuando haya de realizar esfuerzos fuera de lo común podrá disminuirse ese día la cantidad de insulina, o mejor aún, aumentar su merienda o comida. Sus compañeros y el entrenador deberán estar informados de su condición para que puedan prestarle



ayuda de sobrevenir una crisis hipoglicémica inesperada. Como prevención, el niño deberá llevar consigo alguna sustancia glucosada para caso de necesidad.

Bajo ninguna circunstancia podemos permitir que se le restrinja el ejercicio al niño, lo cual además de frustrarle, impide esta extraordinaria forma de disminuir su glicemia, favorecer su crecimiento, y hacerle su vida lo más normal posible.

### Educación

De la información diabetológica que nosotros le hagamos llegar al paciente y sus familiares dependerá nuestro éxito terapéutico, y por ende el futuro del paciente que ha de sobrelevar esta enfermedad de por vida. No bastará con indicar una dieta y prescribir una serie de medicamentos. Habremos de establecer un contacto directo con el paciente y sus familiares y hacerlos partícipes de su manejo.

El lema de la Asociación Panameña de Diabetes "EL DIABETICO QUE MAS SABE ES EL QUE MAS VIVE" encierra la verdad absoluta de la educación diabetológica. El paciente no sólo debe conocer su forma de tratamiento, sino también conocer la enfermedad a fondo, sus complicaciones y la forma de evitarlas. En el caso del niño diabético se debe buscar la forma de que vaya adquiriendo estos conocimientos a la brevedad posible, dentro de sus limitaciones, y en la forma más comprensible. Para poderlo lograr sus familiares también deben adquirir destreza en estos conocimientos. Los mismos han de ser actualizados y revisados por el facultativo, para así reforzarle al paciente y a los familiares lo previamente aprendido.

#### ¿Qué debe saber el niño?

1. Conocimientos básicos sobre la condición.
2. Inyectarse la insulina tan pronto sea posible.
3. Saber realizar las pruebas de orina y el empleo de glucocintas.
4. Conocer los síntomas de hipoglicemia
  - cómo prevenirla
  - cómo tratarla
5. Conocer los síntomas de hiperglicemia.
6. Conocimientos sobre su programa dietético.
7. Conocer los objetivos de su tratamiento.

#### Qué deben saber los padres?

1. Conocimientos básicos de la enfermedad y sus complicaciones.
2. Conocimientos sobre el programa dietético.
3. Realizar las pruebas de azúcar en orina y sangre.
4. Técnica de inyección adecuada.
5. Prevención y tratamiento de reacciones insulínicas.
6. Manejo del niño enfermo.

#### ¿Qué debe saber la maestra?

1. Estar informada que el niño es diabético.
2. Conocer la sintomatología de hipo, e hiperglicemia y su control.
3. No dar sobreprotección al niño.
4. Conocer la dieta y permitir las meriendas y comida a su hora.

Las preguntas antes contestadas son de amplia importancia para el control y tratamiento adecuado del niño. Existen múltiples tipos de ayuda audiovisuales en la forma de

videocintas, folletos, películas y manuales muy útiles para los niños y los familiares. Nos ha dado un resultado excelente una "Cartilla para el Niño Diabético" preparada por nosotros en forma de cuento, en el cual el niño, a la vez que aprende, rellena unos espacios y realiza unos dibujos que le hacen el aprendizaje más agradable. Múltiples compañías de productos para diabéticos pueden facilitar material audiovisual para los mismos.

Como instrumento educativo de gran valor terapéutico no podemos olvidar las Asociaciones de Diabéticos, y los Campamentos Vacacionales para los mismos. En ellos los pacientes se encuentran en sí mismos, ven que no están solos, y pueden demostrarse a sí mismos que pueden sobrelevar adecuadamente su condición.

### Seguimiento del Diabético Controlado

Usualmente después de 7 a 8 días el niño es dado de alta. A la semana de alta del hospital debe de ser reevaluado con glicemia en ayunas y, por lo menos, una glicemia postprandial de dos horas después del desayuno. Su dosis de insulina se modificará según sus glicemias. En dicha cita es muy útil reevaluar la dieta que recibe y el ejercicio que hace, revisando las dudas sobre la enfermedad.

Durante los primeros meses hay que prevenir a los padres sobre la posibilidad de una remisión, vigilando posibles crisis hipoglicémicas.

Todo niño diabético deberá llevar consigo algún tipo de identificación que indique su condición de diabético y su tratamiento. A nosotros nos ha resultado muy útil una tarjeta de identificación en la cual incluimos su dirección, la terapia que está recibiendo, su peso, al igual que datos para una emergencia.

El niño deberá llevar un cuaderno con los datos diarios de su enfermedad, la glucosuria y/o cetonuria, niveles de glicemia, etc. El mismo deberá ser llevado a la evaluación del médico en su visita de seguimiento.

Las visitas de seguimiento se espaciarán según el control del paciente. Nuestros pacientes bien controlados se ven en nuestro consultorio cada dos meses sin problema aparente por esta dilación.

El control del paciente se determinará a base de sus niveles de glicemia, su crecimiento y los niveles de hemoglobina glicosilada. Esta última resulta muy útil para determinar el grado de control del paciente y la efectividad de nuestras indicaciones terapéuticas.

El control del paciente diabético en la actualidad se ha visto muy favorecido por el desarrollo de glucocintas que permiten la dosificación de glicemias instantáneas al minuto. El empleo de refractómetros para determinaciones más exactas de la glicemia, para ser realizadas en la casa por el propio paciente y sus familiares permiten un control clínico más adecuado, a la vez que conciencian más al paciente y sus familiares de su condición. El costo relativamente elevado limita su uso generalizado. En el último año han salido al mercado varios instrumentos de fabricación europea más baratos, al igual que fácilmente manejables y transportables por su pequeño tamaño. Con su abaratamiento se beneficiarán más pacientes de sus bondades.

El tratamiento ideal en la fase aguda y en su trato diario subsiguiente, lo sería el empleo de las bombas de infusión continua y programada. El costo de las mismas limita al presente su utilización, permitiendo su empleo, tan sólo, en un número limitado de pacientes.

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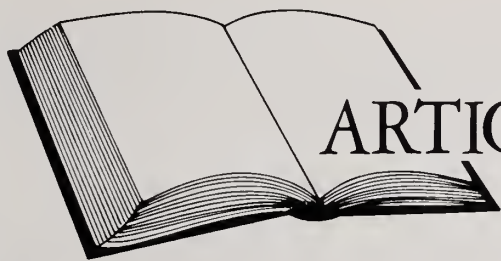
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## ARTICULOS DE REPASO

# Aspiration Pneumonia: Pathophysiology and Treatment

Vidal Vázquez, MSIV  
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**Abstract:** There are three syndromes associated with aspiration of contents into the lungs. These are related to the nature of the aspirate: gastric contents, oropharyngeal bacterial flora and inert substances. Infection has not been shown to play a role in the initial pulmonary complications following aspiration of inert substances or gastric acid, airway obstruction and hypoxia being the most characteristic features. Secondary bacterial infection, however, is a major source of morbidity and mortality. The aspiration of pathogenic oropharyngeal bacteria can lead to the development of necrotizing pneumonia, lung abscess, or empyema. There are differences in the bacteriology of community and hospital acquired respiratory infections, however, both aerobic and anaerobic organisms are involved. Treatment should be established to cover against these organisms.

Aspiration of contents into the lungs causes three syndromes related to the three major aspirates: stomach acid, oropharyngeal bacterial flora and inert substances.

These three aspiration related diseases are: aspiration of acid gastric contents with associated pneumonitis "Mendelson's Syndrome", pleuropulmonary infection, and airway obstruction. It is important to distinguish among these three conditions since they have different therapeutic and prognostic implications. However, a clear distinction often cannot be made since overlapping of the three is often unavoidable.

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### Pathogenesis of Aspiration

Of the mechanisms in the body designed to prevent aspiration, the epiglottis and hiatal sphincter are the most important. Aspiration into the lungs occurs when these mechanisms are impaired or overwhelmed. A change in the state of consciousness as a result of an overdose of a sedative drug, general anesthesia, cerebrovascular accident, cardiopulmonary arrest, a seizure disorder or alcoholic intoxication are the most common causes. Also, the frequency of aspiration problems is increased when a nasogastric tube or tracheostomy is present.

In one study, 45% of normal subjects were noted to have aspirated pharyngeal contents during sleep.<sup>1</sup> Of patients with a depressed sensorium, 70% aspirated pharyngeal contents. These results suggested that aspiration of pharyngeal contents occurred more frequently and more extensively in the patients with depressed consciousness; and that all normal people frequently aspirate secretions from their pharynx during deep sleep.

Pulmonary infections are relatively uncommon among normal subjects. Hence, aspiration of pharyngeal contents alone cannot be blamed for pleuropulmonary infection secondary to aspiration. The type and amount of bacteria aspirated, defense mechanisms and previous damage are among the other factors that contribute to the actual development of infection in aspiration of gastric contents. Incompetence of the hiatal sphincter is the most important factor. Nasogastric tubes produce this incompetence in three ways: first, by physically preventing complete closure of the sphincter, second, by stimulating increased gastric secretion, and third, by giving the clinician the possibly false impression that the patient's stomach is empty. Excessive intragastric pressure also makes hiatal incompetence likely. Excessive mask ventilation during resuscitation or anesthesia can insufflate the patient's stomach with gas and promote regurgitation. Morbidity obese patients can also have elevated intra-abdominal pressure.

Aspiration of particulate matter leads to obstruction of bronchi, which causes a loss of lung volume followed by circulatory shunting. Most foreign bodies enter the right main-stem bronchus because of its more direct alignment with the trachea. If small enough, the particles tend to move into the most dependent segment of the lung. In the supine patient, this is often the posterior segment of the upper lobe or the superior segment of the lower lobe.

Finally, aspiration of irritating food, such as partially digested animal or vegetable products, will initially cause an extensive hemorrhagic pneumonia, followed in a few days with a focal granulomatous reaction around the food particles.

### Aspiration of Gastric Acid and Inert Fluids

In 1920 the toxic effect of acid on the lung was reported in an experimental animal study.<sup>2</sup> Subsequently, the aspiration of gastric contents in humans was described by Mendelson in a clinical study of 66 obstetrical patients who aspirated during anesthesia.<sup>3</sup>

The entity known as "Mendelson's Syndrome" was initially described in 61 of the patients who aspirated liquid gastric contents and developed acute respiratory distress and bronchospasm. All these patients had chest X ray film changes consisting of irregular densities in the right lower lobe or both lower lobes. Infection was considered a secondary complication. Twenty patients were febrile and eight eventually developed bacterial pulmonary infection.

The characteristic physiologic feature in "Mendelson's Syndrome" is hypoxia in association with a normal or low PCO<sub>2</sub> indicating ventilation-perfusion disturbances. Pulmonary function tests indicate reduced compliance related to edema, hemorrhage and microatelectasis. These patients can progress to the adult respiratory distress syndrome.

The pH appears to be a crucial factor in reproducing the disease. Using graded doses of hydrochloric acid, there is no toxic reaction with a pH above 2.4. The extent of pathology is inversely related to the pH below this level. Experimental animal studies have shown that the toxic effects of acid are immediate and extensive.<sup>4</sup>

The treatment of hypoxia of "Mendelson's Syndrome" involves the correction of hypoxia with oxygen and assisted ventilation. Steroids are often recommended. In theory, steroids should limit the severity of tissue destruction after aspiration and help alleviate bronchospasm. However, laboratory and clinical studies measuring improvement of oxygenation, as well as cardiovascular integrity, do not show any improvement in short-term or long-term morbidity or mortality statistics from low or high doses of steroids.<sup>5</sup>

The role of antibiotics in acid pneumonitis is controversial. Most observers agree that infection plays little or no role in the initial pulmonary complications following aspiration of either inert fluids or gastric acid.<sup>6,7</sup> In the first few days after gastric acid aspiration, however, the injured lung is presumably quite vulnerable to bacterial infection.<sup>6,7</sup> Some bacteria, no doubt, are washed into the tracheobronchial tree from the oropharynx or stomach at the time inert or toxic aspirates enter. However, in the absence of hypochlorhydria or gastrointestinal motility disturbances, gastric contents appear to contain few, if any bacteria. The reason for this is not clear, but it is possible that bacteria in oropharyngeal secretions either do not always gain entry to susceptible areas or are diluted by the aspirate to concentrations insufficient to overwhelm local defense mechanisms.

If antibiotics are used, it is necessary to appreciate that their role is secondary to the more compelling and immediate considerations of aggressive respiratory support, tracheal suction, and intravenous fluids. Antimicrobials may be given initially on the premise that infection is likely, and prophylaxis with its attendant risks is justified. Most authorities conclude that antibiotics should be reserved for cases in which there is evolving evidence of infection such as significant fever, purulent sputum, leukocytosis and progressive infiltrates. There is little evidence that early use of antibiotics actually prevents subsequent infection, but it is clear that these drugs will select a more resistant bacterial flora.<sup>6</sup> Whether antibiotics are used

for prophylaxis or actual therapy, the selection of agents should take into account that these events usually occur within a hospital, and likely pathogens include aerobic gram-negative bacilli as well as the usual oropharyngeal bacteria.

### Aspiration of Pathogenic Bacteria

In the pre-antibiotic era the course of aspiration of bacteria was documented.<sup>8,10</sup> The initial lesion was pneumonitis and the symptoms in the early stages were often mild. After 8-14 days there was a tendency to observe tissue necrosis with abscess formation or extension to the pleural space. Putrid discharge and cavitation on chest x ray examination were not present until this later stage of disease.

Patients seen early in their course will have roentgenographic evidence of pneumonitis which may resemble other forms of bacterial pneumonia but the distinctive features are the more insidious onset and an underlying illness which predisposes to aspiration. Favored anatomic sites of involvement are those subject to gravitational flow; the posterior segments of upper lobes or superior segments of lower lobes with are dependent in the upright position.<sup>6</sup> Patients who are observed later in the course of the process, one to two weeks after aspiration, are likely to have cavitation or empyema formation.

The aspirated inoculum is composed largely of oropharyngeal secretions, especially saliva containing bacteria pooled from the tongue, gingiva, buccal mucosa and pharynx. Gastric contents may also be aspirated and the bacteria from this source, if any, are similar to those of the upper respiratory passages.<sup>6</sup> Quantitative culture of saliva yield approximately 10<sup>8</sup> bacteria/ml with anaerobes outnumbering aerobes and facultative bacteria by a factor of 5-10 to 1.<sup>6,11</sup> In terms of specific bacteria the flora is extremely complex. Rosebury<sup>11</sup> lists 21 different genera of bacteria which are considered normal cohabitants of the upper respiratory tract passages. Organisms which become of greatest importance in terms of pathologic potential are anaerobic *Streptococci*, *Fusobacteria* and *Bacteroides melaninogenicus*. Enteric, gram-negative bacilli or *Pseudomonas* and *Serratia* species are rarely found in the oropharyngeal flora of nonhospitalized persons.<sup>12</sup> Studies have shown that the oropharynx of hospitalized patient is commonly colonized with gram-negative aerobes and facultative anaerobes, which cause many nosocomial respiratory infections.<sup>12</sup> Gram-negative bacilli had been the predominant isolates (around 70%) of the hospital-acquired aspiration pneumonia,<sup>12</sup> but more than one third of these cases also showed anaerobes. These findings indicate that anaerobic bacteria are common pathogens in aspiration pneumonia, including pneumonia that occur in hospitalized patients. Table I shows the common isolates in aspiration pneumonia including both aerobic and anaerobic organisms.

*Bacteroides fragilis* is not found in the upper respiratory tract of healthy individuals.<sup>12</sup> But this organism had been found in 13% of the patients reported by Lorber and Swenson<sup>12</sup> and in 17% of the patients reported by Barlett, Gorbach, and Finegold.<sup>13</sup> To date this apparent contradiction is unexplained. Sick persons may have an alteration in the anaerobic flora of the oropharynx that is analogous to the alterations seen the aerobic flora. Whatever the reason this finding may be clinically significant regarding the treatment.

In contrast to patients with the others two types of aspiration there is no debate about the role of infection or the



necessity of antimicrobial therapy in patients with the syndrome of aspiration of pathogenic oropharyngeal bacteria. The antimicrobial therapy is optimally based on cultivation of a reliable specimen source. Expecterated sputum is unsuitable since these specimens are invariably contaminated by oropharyngeal bacteria during passage through the upper airways. Transtracheal aspiration and aspiration of empyema fluid with aerobic and anaerobic cultures are perhaps the preferable approaches. Cultures of an organism from blood would be highly suggestive in the proper clinical milieu. The implication is that unless there is bacteremia or empyema, a transtracheal aspiration is required to establish a bacteriologic diagnosis.

Anaerobes have been shown to be the predominant pathogens in the majority of cases of community-acquired aspiration pneumonia. Importantly, it has also been demonstrated that most of these patients respond satisfactorily to treatment with penicillin alone provided therapy is prolonged.<sup>7</sup> This response occurs despite mixed infection with organisms such as *Bacteroides fragilis* which are resistant in vitro to penicillin. Thus, with its low cost and minor risk of toxicity, penicillin is regarded by most as the drug of choice for community-acquired, aspiration related chest infections. For allergic patients, clindamycin is an appropriate alternative.

In contrast, case acquired during hospitalization are likely to involve facultative gram-negative bacilli or *Staphylococcus aureus*, as well as anaerobic bacteria. Empirical selection of antibiotics in this setting should include a combination of agents to provide activity against both the aerobic and anaerobic components of the infection. The choice for most authorities is an aminoglycoside in combination with a semisynthetic penicillin (oxacillin or nafcillin), clindamycin or a cephalosporin.

TABLE I

Common Isolates in Aspiration Pneumonia	
Aerobes	Anaerobes
Gram-positive cocci	Cocci
Staphylococcus aureus	Peptostreptococcus
Streptococcus pneumoniae	Peptococcus
Gram-negative bacilli	Gram-negative bacilli
Klebsiella	Bacteroides
Pseudomonas aeruginosa	melaninogenicus
E. coli	Fusobacterium
Enterobacter cloacae	nucleatum

#### Aspiration of Inert Substances

The aspiration of inert substances or inert particles may result in airway closure. The volume of lung involved determines the severity of the clinical presentation.

Endoscopic evaluation of the tracheobronchial tree with visualization of a foreign body provides definitive diagnosis. Patients with mild symptoms resulting from aspiration of a foreign body may show obstructive hyperinflation, with shifting of the mediastinum, on inspiration-expiration x-ray films of the chest. There may be atelectasis and varying degrees of respiratory insufficiency. Occasionally, the condition goes on to pulmonary infection as a result of obstructive pneumonitis. Bacterial infection often follows if particulate material in the lower respiratory tract is not removed within one to two weeks.<sup>6</sup> The types of infectious complications include pneumonitis (often recurrent), bronchiectasis, lung abscess and empyema. Thus, there are two distinctive periods in which these patients are likely to seek medical attention, the early obstructive or irritative phase and a later stage characterized by bacterial complications.

The primary therapy for aspiration of an inert substance or foreign body is clearance of the tracheobronchial tree. This can be accomplished readily with a fiberoptic bronchoscope, but the removal of large foreign bodies occasionally requires the rigid bronchoscope.

Suctioning assists in the removal of particulate matter both directly and by inducing cough. If lavage must be performed to remove particles, only a small quantity of fluid should be used.<sup>14</sup>

It is important to re-emphasize that infection has not been shown to play a role in the initial pulmonary complications following aspiration of either inert or toxic substances. Secondary bacterial infection, however, especially gram-negative bacillary pneumonia, is a major source of morbidity and mortality. One who elects to use prophylactic antibiotics in this setting must weight unproved benefits against potential risks. If therapy is withheld but appropriate clinical and microbiological findings subsequently indicate that infection has supervened, then specific therapy can be given in a rational fashion. In patients in whom necrotizing pneumonia, lung abscess, or empyema develops following aspiration of pathogenic oropharyngeal bacteria, one should be cognizant of the differences in the bacteriology of community versus hospital settings.

**Resumen:** Hay tres síndromes que se asocian con la aspiración de contenidos a los pulmones. Estos están relacionados con la naturaleza del aspirado: contenido gástrico, la flora bacteriana de la orofaringe, y las sustancias inertes. La infección no es un factor importante en las complicaciones pulmonares iniciales al aspirar sustancias inertes o contenido gástrico. Las características más prominentes son la obstrucción de las vías respiratorias y la hipoxia. Sin embargo, la infección bacteriana secundaria es una causa importante de morbilidad y mortalidad. La aspiración de bacterias de la orofaringe puede causar el desarrollo de pulmonías necrotizantes, abscesos pulmonares o empiema. Hay diferencias entre la bacteriología de las infecciones del tracto respiratorio nosocomiales y las adquiridas en la comunidad, sin embargo, tanto los organismos aeróbicos como anaeróbicos están envueltos. El tratamiento que se establezca debe tener actividad contra estos organismos.

#### Acknowledgment

We want to thank Ms. Carmen Noelia Colón Sifontes for the invaluable secretarial assistance in the preparation of this paper.

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# SIRVIENDO AL PUEBLO Y A LA PROFESION MEDICA



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# Pharmacokinetics of Hydralazine and the First Pass Effect

Robert J. Holt, Pharm. D.  
John D. Gaskins, Pharm. D.

**Abstract:** Pharmacokinetics, a discipline new to the health sciences, has immensely increased our knowledge of drug behavior in both the research and clinical areas. Clinical pharmacokinetic services are functioning on a day to day basis in many patient care areas, with well defined kinetic models existing for several drugs; such as the aminoglycosides, digoxin, lithium, quinidine, and phenytoin. However, there are still many drugs that do not readily fit into even the most complex schemas. Here, we describe the state of the art of one of these drugs, hydralazine, and its' major metabolic stumbling block, the first pass effect.

## Enterohepatic Metabolism (First Pass Effects)

In order to better understand the pharmacokinetic properties of drugs, one must first begin by classifying drugs as either enteral or parenteral. An enteral or hepatic route is when the drug enters a section of the gastrointestinal tract by way of sublingual, intraperitoneal, rectal or oral dosing, prior to reaching the systemic circulation. Parenteral routes such as subcutaneous, intrathecal, intravaginal, topical, intramuscular and intravenous, enter the peripheral circulation directly.<sup>1</sup> In order to achieve a maximally effective blood level for a drug, the route of administration should be selected carefully.<sup>1</sup> This is particularly true for those drugs susceptible to metabolism while passing through a barrier such as the lung mucosa, intestinal wall or the liver.<sup>2</sup> Those drugs entering the hepatic route will undergo substantial biotransformation before reaching the systemic circulation. Drugs given orally are particularly prone to this. The drug molecules will cross the intestinal wall where they are collected by the mesenteric veins. They then pass into the hepatic portal vein directly into the liver, where most drug metabolism occurs before reaching the peripheral circulation.<sup>1, 2</sup> This phenomenon is generally referred to as the "first-pass effect". However, metabolic loss during first-pass is not necessarily confined to drugs given enterally. Bronchodilator drugs such as isoproterenol are metabolized during absorption across the lung mucosa before entering the systemic circulation. Extensive protein binding at the site of administration is another kind of first-pass barrier that can diminish the effectiveness of drugs such as phenytoin and digoxin when they are given intramuscularly.<sup>2</sup> Harris and Riegelman have shown that p-aminohippuric acid (PAH) will undergo a first-pass effect when given by renal infusion.<sup>3</sup> Therefore, the term used for the hepatic first-pass effect has

come to be known more accurately as enterohepatic metabolism. However, since the latter first-pass phenomena mentioned are minimal when compared with enterohepatic metabolism, the two terms are generally used interchangeably.

Dose requirements are sometimes larger for a drug given orally, as compared to the same amount of drug given parenterally. This is often the case despite complete and rapid absorption of the drug and is attributed to enterohepatic metabolism. It is important to remember the distinction between absorption and availability. *Absorption* is the loss of material from one bulk phase arising from the movement into another, whereas *availability* is the extent to which the administered drug reaches some point of measurement. Aspirin, salicylamide, and lidocaine are all well absorbed, yet poorly available when given orally.<sup>3, 5</sup> Again this is due to the first-pass effect on the drugs as they cross the gut wall and enter the liver before reaching the systemic circulation. Dollery et al<sup>1</sup> attributed the 1000 to 1 ratio of intravenous to oral chronotropic potency of isoproterenol in man to the formation of an inactive ethereal sulfate during enterohepatic metabolism. Oral chlorpromazine, propranolol, hydralazine and phenytoin are also largely metabolized during first-pass.<sup>1, 3</sup>

For those drugs subject to first-pass metabolism one must consider the condition of the liver to avoid dosing problems. In a patient with a diseased liver the dose of the drug is usually lowered accordingly. Uremic patients receiving drugs that are highly protein bound (i.e phenytoin) may need to increase their dosages. This is because of increased metabolism resulting from decreased plasma binding of the drug.<sup>6</sup> Genetic predisposition may, also, play a role in the rate of first-pass metabolism in some drugs, such as hydralazine. Phenobarbital is known to induce the metabolism of other drugs in the liver, requiring in most cases an increase in dosage. One must also realize that in drugs with a low therapeutic index a higher incidence of side effects is likely to occur with the oral form, since higher doses must be given to attain effective blood levels.

Loss of the parent drug during the first-pass effect limits the initial availability of the drug, but does not influence the elimination of the drug once it is in the systemic circulation. A drug metabolized extensively during passage through the liver may still have a long half life in the plasma, if it has a large volume of distribution.<sup>1</sup>

The rate at which the drug is delivered to the liver can influence the fraction of the administered dose which reaches the fluids of distribution.<sup>7</sup> A decrease in liver blood flow results in an increase in the extent of first-pass metabolism.<sup>2</sup> The extent of extraction of the drug by the liver is controlled not only by Michaelis-Menten kinetics, but also by the concentration of drug passing the liver per unit time. For drugs highly cleared by the liver the low oral availability should be associated with a rapid rise in metabolite levels. Again phenytoin is an example of this, as ninety-five percent is metabolized into the inactive metabolite 5-phenyl-parahydroxy-diphenylhydantoin (HPPH).<sup>7</sup> High doses of lidocaine will cause dizziness as a result of high concentrations of its' metabolites.<sup>7</sup> High metabolite concentrations are, also, seen following oral doses of salicylamide and isoproterenol.<sup>7</sup>

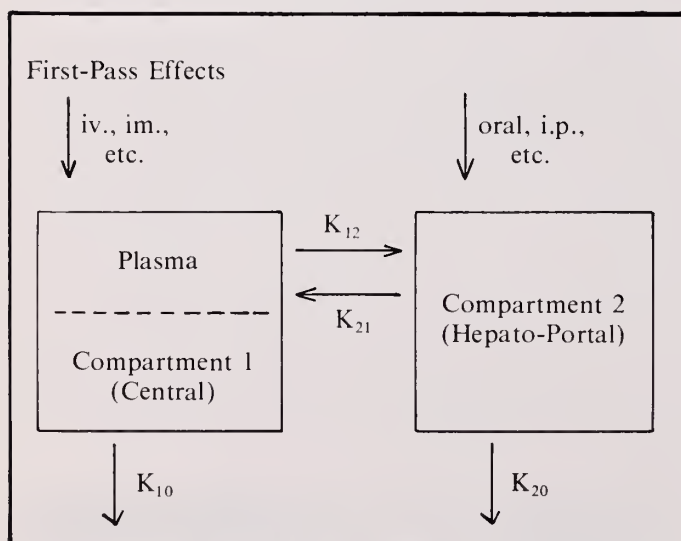
First-pass effects influence body clearance, too. As the extent of first-pass metabolism increases, the reliability of urinary clearance as an index of hepatic elimination decreases. Therefore, these changes must be reflected quantitatively by changes in the area under the plasma concentration-time

curve. The law of corresponding areas is used to assess the percent of absorption by comparing the relative areas under the plasma concentration time curves after oral and intravenous administration.<sup>3</sup>

Table one is a compartmental model describing the time course of first-pass drugs and their metabolites in the body.<sup>8,10</sup> Elimination is assumed to occur in part from a compartment distinct from that containing the vascular sampling site. It is analogous to the hepatoportal system receiving the drug directly through portal vein infusion or administration by a route in which the drug reaches the systemic circulation via the portal vein.<sup>8</sup> As with other drugs, pharmacokineticists have developed mathematical equations to help us better understand the pharmacodynamics of drugs undergoing first pass metabolism. The following equation is one that can serve as a practical tool in analyzing the first-pass phenomenon.<sup>8,9</sup>

$$F = 1 - \frac{D}{QL(Auc)_{IV}}$$

TABLE ONE



First-pass pharmacokinetic models. The rate constants  $K_{20}$  and  $K_{10}$  characterize hepatic metabolism and urinary excretion, respectively. The central compartment includes all accessible body compartments except the liver.

This equation is used to predict systemic availability ( $F$ ) after oral administration of such drugs as propranolol, propoxyphene, and alprenolol.<sup>2,10,11</sup> Substitution of the IV dose ( $D$ ) and the respective total area under the drug level time curve ( $AUC$ ), as well as the blood flow rate to the liver ( $QL$ ) should yield an estimate of the extent to which the first-pass effect contributes to a reduction in the curve after oral administration, relative to that observed after peripheral IV administration.<sup>8,9</sup> Harris<sup>3,8</sup> found that the area under the plasma concentration time curve of aspirin upon administration of the drug into the hepatic portal vein was 54-78% that observed after administration of equivalent doses via the vena cava. Despite complete drug absorption, the area under the plasma level time curve after oral administration may be considerably less than the corresponding area following IV administration.<sup>8</sup> One should use caution in applying the law of corresponding areas in the assessment of drugs absorption, especially from the gastrointestinal tract. However, by taking into consideration the possible clearance and metabolic processes ("first-pass effect") within the gastrointestinal tract and hepatic

tissues, and by using the special equation provided, one can estimate the physiologic availability of enteral dosage forms.<sup>3,4,5,8</sup>

Although the mathematical expression used to explain and quantify first-pass changes are not readily available for clinical utility, they nonetheless can be of considerable research interest.

In the second part of this article we offer a pharmacokinetic monogram of hydralazine, a drug which undergoes extensive enterohepatic metabolism.

### Hydralazine

Hydralazine hydrochloride is a phthalazine derivative antihypertensive. Its hypotensive effect comes from reducing peripheral resistance by a direct vasodilatory effect on vascular smooth muscles.<sup>12,13,14</sup> Diastolic blood pressure is normally more reduced than the systolic.

It is most commonly used in combination with the Beta blockers. In particular, combined antihypertensive therapy with propranolol has been shown to be quite effective in minimizing hydralazine-induced tachycardia.<sup>4</sup> Recently, its unapproved usage in the treatment of congestive heart failure has become increasingly popular.<sup>15,16</sup>

### Absorption

Hydralazine is rapidly and almost completely absorbed from the gastrointestinal tract (52-90%). Some of the drug (6-10%) is excreted into the small intestine via the biliary tract. However, most of the drug (80%) is rapidly excreted in the urine primarily as non-active metabolites. Onset of effect of intravenously administered hydralazine occurs in 5-15 minutes with a peak effect in 10-80 minutes.<sup>18</sup> Orally administered drug effects occur within one hour and the duration of effect after multiple oral doses may be in excess of 30 hours.<sup>17</sup> Higher peak drug concentrations are achieved among slow acetylators than for fast acetylators.<sup>19,21</sup>

### Bioavailability

Acetylator status appears to be the main determinant of bioavailability. Bioavailability expressed as area under the serum concentration-time curve is significantly greater for slow acetylators than fast acetylators. Bioavailability, also, depends on the rate of dissolution.<sup>22</sup> Slow release 50mg tablets were found to be much less bioavailable than a rapidly disintegrating tablet in slow acetylators. This suggests a capacity limited metabolism of hydralazine. The bioavailability of an oral dose was only 26-55% of an identical IV dose. Taking into account the absorption of up to 90% of an oral dose leaves a substantial fraction of the oral dose to be accounted for in terms of first-pass metabolism.

### Protein Binding and Apparent Volume of Distribution

Hydralazine is reported to be approximately 88-90% bound to plasma proteins.<sup>21</sup> Animal studies indicate that hydralazine is widely distributed in body tissue. Apparent volumes of distribution have been reported from 0.29L/Kg to 2.24L/Kg with an average of 0.45L/Kg.<sup>22,28</sup>



## Metabolism

Hydralazine undergoes extensive enterohepatic metabolism. It is metabolized in the intestinal wall during absorption and in the liver by acetylation, hydroxylation and conjugation with glucuronic acid. Four metabolites have been identified. N-acetylation accounts for approximately 60% of the absorbed drug's metabolism.<sup>24</sup> First-pass acetylation in the intestinal wall and liver is related to the genetic acetylator phenotype. The first-pass effect appears to be a capacity limited process (follows non-linear kinetics).<sup>25</sup> The terminal elimination half-life is independent of both the size of the dose and the area under the curve (total absorption) obtained. Since the major mode of elimination is N-acetylation one would expect a clear cut difference in the way slow acetylators and fast acetylators handle the drug. Some authors have demonstrated differences in peak serum concentrations. However, Talseth<sup>24</sup> states that differences in the terminal elimination half-life have not been demonstrated. He explains that if N-acetylation is the principal route of metabolism, a bimodal polymorphic and monomorphic N-acetylation may occur in man. The rather uniform elimination rate of the drug among fast and slow-acetylators might indicate that monomorphic N-acetylation governs the elimination rate in the post distributive phase. And since polymorphic N-acetylation operates at a normal rate, even in renal failure, this would provide a possible explanation for the the unexpected accumulation of hydralazine observed in uremic patients.

A small amount (6%) of the drug is converted to a hydrazone, which may be responsible for some toxic effects.

## Renal Excretion

Hydralazine and its metabolites are rapidly excreted by the kidney and 80% of an oral dose appears in the urine within 48 hours.<sup>21</sup> It was reported by Zak et al. that the urinary excretion of unchanged hydralazine was independent of the route of administration.<sup>26</sup> However, in a study by Talseth<sup>23</sup> after intravenous injection of 0.3mg/kg, 11 to 14% of the dose was excreted unchanged, compared with only 2 to 4% after oral ingestion of an identical dose.

## Elimination Half-Life

The elimination rate of hydralazine from the plasma does not show a clear cut difference between rapid and slow acetylators of the drug, although it tends to be more prolonged in slow acetylators. In patients with normal renal function, the plasma half-life is 1.7 to 3.0 hours. However, in the presence of chronic renal failure, the plasma half-life is markedly prolonged from 7 to 16 hours.<sup>27</sup>

## Clinical Pharmacokinetics in Disease States Steady State Plasma Concentrations in Hypertensive Patients

When using hydralazine in the treatment of hypertension, it is necessary to establish the acetylator phenotype of the patient in order to evaluate the therapeutic response. In three studies, it was shown that following the same oral daily dosage, slow acetylators attained higher plasma levels of hydralazine than rapid acetylators of the drug.<sup>20 28 29</sup>

Zacest and Koch-Weser found a plasma concentration to daily dose ratio, which was 1.7 times higher among slow acetylators than among fast acetylators.<sup>20</sup> Therefore, to produce identical blood concentrations of hydralazine in fast and slow acetylators, about twice as much of the drug must apparently be given to fast acetylators when employing a divided dose schedule of 25mg 3 or 4 times daily.<sup>24</sup> At moderate doses, the possibility of saturable first pass elimination of the drug does not enter the picture. However, doses greater than 25mg in slow acetylators or above 100mg in fast acetylators may lead to a disproportionately large increase in the amount of unchanged hydralazine appearing in the systemic circulation, as a consequence of capacity-limited first-pass metabolism (N-acetylation of the drug).<sup>24</sup>

## Effect of Chronic Renal Failure

With only 7% of the unchanged drug excreted in the urine one would not expect accumulation of hydralazine in renal failure.<sup>25 30</sup> Surprisingly, hydralazine does accumulate in the uremic patient as demonstrated by Talseth,<sup>27</sup> who showed a markedly prolonged half-life of 15.8 hours (creatinine clearance 16ml/min). Therefore, a close correlation between the glomerular filtration rate and the elimination half-life of hydralazine was proven.<sup>27</sup>

Talseth also showed that a group of hypertensive patients with creatine clearances below 30ml/min., had steady state serum concentrations 4-5 times higher than corresponding concentrations among hypertensive patients with normal renal function.<sup>27</sup> The therapeutic implications of accumulation of hydralazine in uremia is not known, because there have been no reports of toxicity.

## Correlation Between Pharmacokinetics and Circulatory Effects

The duration of the hypotensive effect of hydralazine exceeds that predicted from the rate of elimination of the parent compound from the plasma, and successful treatment of hypertension with twice daily dosage schedules has been reported.<sup>19 31 32</sup> It was further demonstrated by these authors that the half-life for the return of blood pressure toward pretreatment levels after cessation of 2 week treatment in four patients amounted to 30 to 140 hours (mean 97.5). From these observations it is not likely that a simple relationship exists between the concentration of hydralazine in blood and the circulatory effects of the drug.

The controversy has yet to be resolved whether serum concentrations correlate to the magnitude of its hypotensive effect.<sup>20 28 29</sup> Currently, the routine measurement of hydralazine in the blood does not appear to be useful in the clinical management of patients.

## Systemic Lupus Erythematosus Syndrome (SLE)

The chronic administration of hydralazine can lead to a syndrome resembling the acute rheumatoid state or, when fully developed, disseminated lupus erythematosus. The incidence of this form of hydralazine toxicity approaches 10 to 20% in individuals treated with 400mg per day or more; with doses under 200mg daily it has only rarely been reported, but

has occurred at doses of 100mg daily.<sup>33 34</sup> The syndrome is almost always associated with circulating antinuclear antibodies and is more common in caucasians and slow acetylators of the drug.<sup>35</sup> This may be due both to the higher and more prolonged plasma levels that are achieved in slow acetylators and the fact that such individuals appear to have a predisposition to the development of lupus.<sup>36</sup> The syndrome is completely reversible upon discontinuance of the drug. However, the antinuclear antibody may persist for 10 years or longer.<sup>33</sup>

Acetylator phenotyping is useful for identifying patients at risk of developing hydralazine SLE. Such individuals are slow acetylators, most often females, who have been treated with hydralazine for more than 6 months.

### Conclusion

Hydralazine is an example of a drug whose pharmacokinetic analysis is complicated by enterohepatic metabolism. Its pharmacodynamics can be better understood, however, by applying general pharmacokinetic principles to better utilize this and other drugs undergoing first-pass effects.

**Resumen:** Farmacocinética, una disciplina relativamente nueva en las ciencias de la salud, ha aumentado inmensamente nuestros conocimientos sobre el comportamiento de drogas tanto en el área de investigación como clínica. Existen servicios de farmacocinética clínica que funcionan regularmente en diferentes áreas del cuidado, a paciente, con modelos cinéticos bien definidos para varias drogas; como los aminoglicósidos, digoxina, litio, quinidina y fenitoina. Sin embargo, todavía hay muchas drogas que no se ajustan fácilmente aún a los esquemas más complejos. Describimos en este artículo una de esas drogas, hidralazina, la cual sufre extensos cambios metabólicos debido a su primera biotransformación.

### Acknowledgement

The authors would like to acknowledge Luz M. Gutiérrez, Pharm. D. and Sandra Vargas, Pharm. B.S. for their assistance in the preparation of this paper.

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# Aspectos Clínicos y Fisiológicos de Corrientes de Alto Voltaje\*

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**D**urante los últimos años el uso de corrientes eléctricas de alto voltaje se ha popularizado grandemente en muchos departamentos de fisioterapia de hospitales y médicos en los Estados Unidos hasta el punto de que ha desplazado el uso del ultrasonido, la diatermia y otras modalidades. Entre las razones que tenemos para esto es que los aparatos de alto voltaje han resultado más efectivos que los aparatos convencionales de bajo voltaje debido a la mayor penetración, mejor tolerancia por el paciente y mejor estimulación de los nervios y músculos por estas corrientes.

Cuando decimos alto voltaje, nos referimos a intensidades de más de 150 voltios. Tengamos en cuenta que el voltaje que encontramos en la corriente que se obtiene regularmente de los receptáculos eléctricos en nuestros edificios es de 120 voltios. Sabemos que el uso de esta corriente o la que se obtiene de los estimuladores convencionales de bajo voltaje resulta un tanto desagradable y poco aceptable por el paciente promedio. Sin embargo, la estimulación obtenida con el uso del EGS, (electro-galvanic-stimulator) o estimulador de alto voltaje, resulta en una sensación relativamente agradable cuando se usan las intensidades terapéuticas. Esto se debe a que la duración de la honda que se usa es extremadamente corta, de menos de cien microsegundos de duración. Esta duración, como sabemos, no es suficiente para estimular las fibras nerviosas que conducen la sensación de dolor. No discutiremos en detalle los aspectos técnicos de las corrientes eléctricas ya que como médicos estamos más interesados en los aspectos clínicos y fisiológicos relacionados con estas corrientes.

Ultimamente se han conducido investigaciones clínicas las cuales han demostrado tanto la efectividad como el modo de acción de esta modalidad en el tratamiento de varias condiciones entre las que tenemos:

1. Dolores: agudos o crónicos, ya sean de origen muscular, articular, tendinoso o neurológico.
2. Edema: post-quirúrgico o traumático.
3. Atrofia Muscular: por desuso o por denervación.
4. Espasticidad o espasmos musculares
5. Úlceras: decúbitas o de origen vascular o diabético.
6. Prevención de la tromboflebitis post-quirúrgica.
7. Disfunción temporomandibular.

Tratemos primero los efectos químicos y fisiológicos y como es que estos quizás puedan ayudarnos a entender o a elucidar algunos de los resultados terapéuticos obtenidos en estas condiciones.

**Efectos químicos:** La aplicación de una corriente galvánica a través de una solución de electrolitos produce una migración de iones o sea, partículas cargadas eléctricamente hacia polos opuestos. Cuando estos iones llegan al polo opuesto, ocurren

ciertas reacciones químicas específicas (iontoforesis). Cuando el  $\text{Na}^+$  migra hacia el cátodo se neutraliza al ganar electrones y con el agua forma la base  $\text{NaOH}$  que aumenta la alcalinidad de los tejidos. El  $\text{Cl}^-$  por su parte, migra hacia el ánodo, se combina con el hidrógeno  $\text{H}^+$  y produce el ácido  $\text{HCl}$ . Entre otras cosas esto produce irritación en los tejidos y la liberación de histamina que a su vez produce vasodilatación. Por eso es que después de un tratamiento notamos que la piel se ha enrojecido. Esta vasodilatación seguramente ayuda en el tratamiento de úlceras y en la unión de fracturas que no unen.

Estas corrientes también producen la migración de ciertas moléculas coloidales como las grasas y las proteínas hacia el polo negativo (cataforesis). La alcalinización que se produce en la región del cátodo disuelve las proteínas y esto causa que los tejidos se ablanden. La acidez que se produce en la región del ánodo causa que las proteínas se coagulen y por consiguiente que los tejidos se endurezcan.

Estas reacciones fisicoquímicas producen resultados secundarios específicos que incluyen efectos bacteriostáticos y bactericidas. Rowley<sup>1</sup> en 1972 en estudios con *E. coli* in vitro y Wolfcott<sup>2</sup> en estudios clínicos demostraron el efecto bactericida del polo negativo. Los mecanismos que producen estos no han sido completamente elucidados pero se presume que las corrientes interfieren con la actividad intracelular de estos organismos.

**Efectos fisiológicos:** Con estimulación eléctrica a músculos que están paralizados, débiles o inactivos, podemos producir contracciones fuertes que evitan el estancamiento de la sangre venosa que se observa en estos casos y que causa la tromboflebitis post-quirúrgica. La estimulación eléctrica de los músculos de las extremidades inferiores se ha probado evita la tromboflebitis en los casos post-quirúrgicos a través del efecto de bombeo de los músculos que ayuda al regreso de la sangre al corazón.

La estimulación eléctrica también produce, como sabemos, reflejos autonómicos a través de la excitación directa de las neuronas aferentes de las raíces dorsales produciendo vasodilatación periférica.

Así vemos tres métodos por los cuales la estimulación eléctrica puede aumentar la circulación: 1. Químicamente a través de la acumulación de metabolitos y la producción de histamina. 2. Mecánicamente a través de la contracción muscular con su efecto de bombeo. 3. Neurológicamente a través de la excitación de nervios aferentes autonómicos que causan vasodilatación.

## Aplicaciones Clínicas

Aunque el uso de corrientes eléctricas fue desarrollado hace muchos años, solamente recientemente es que se han hecho investigaciones científicas con respecto a la efectividad de esta modalidad en condiciones específicas.<sup>3 4 5</sup> Nuevas indicaciones para el uso de corrientes han surgido debido a los nuevos conocimientos sobre los efectos de la electricidad en los diferentes tejidos del cuerpo. Pero la verdad es que todavía hace falta más información de como estas corrientes surten sus efectos, o sea el mecanismo de acción. La mayoría de las investigaciones clínicas se han hecho con generadores de bajo voltaje, sin embargo, los generadores de alto voltaje son los que están ganando popularidad. Estas corrientes penetran más y son más selectivas para la estimulación y reclutamiento de las fibras de diámetro grande, por esto trabajan mejor y son más efectivas.

Un área de investigaciones clínicas con corrientes eléctricas que ha producido resultados dramáticos ha sido la que

\* Conferencia dictada a la Sección de Medicina Física y Rehabilitación de la Asociación Médica de P.R., 20 de mayo de 1982.

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trata con la reparación y el crecimiento del hueso y otros tejidos. Se han demostrado los efectos beneficiosos en la cicatrización de fracturas (non-union), heridas y úlceras indolentes.<sup>2 4 6</sup> Tanto fracturas como úlceras y heridas que no han cicatrizado con los métodos usuales han sanado con el uso de la estimulación eléctrica en muchas ocasiones. Los mecanismos que trabajan o influyen en estos casos no han sido establecidos definitivamente pero se cree que estos incluyen: el aumento de la circulación, los efectos bactericidas y/o bacteriostáticos y otros efectos que estimulan probablemente directamente la reparación y/o regeneración de los tejidos. Diferentes estudios han demostrado que tanto el polo negativo como el positivo puede estimular el proceso de cicatrización. Se han usado para esto diferentes clases de corrientes y electrodos, algunos invasivos dentro de los mismos tejidos, corrientes directas o alternas, constantes y pulsantes y PEMF (campos electromagnéticos pulsantes).

Otra área de investigaciones es en la reducción de edema. Sabemos que en los casos de trauma a los tejidos el edema resulta debido a la acumulación de fluido en el espacio intersticial debido a la desorganización y la traumatización de las membranas. Esto permite la migración de las proteínas y las células y el desplazamiento del fluido. Tanto las proteínas como las células tienen una carga positiva y se puede inferir que si aplicamos una corriente con el polo negativo en la proximidad de estas, esto puede repelerlas fuera del área donde se aplica la corriente. Otra inferencia que se puede hacer es que la corriente pueda estimular directamente los nervios simpáticos que causan vasoconstricción y por consiguiente reducir la acumulación del fluido en el área.

El modo de acción para el alivio del dolor todavía no se ha determinado totalmente y dependemos enteramente de la experiencia clínica. Nuestra experiencia clínica nos lleva a la conclusión de que los resultados en esta área son mucho más efectivos que con las otras modalidades que usamos en el Departamento de Medicina Física. Richard Herman<sup>7</sup> en sus investigaciones clínicas opina que la estimulación a través de esta modalidad produce un aumento en la serotonina que es un factor o transmisor neuro-químico implicado en el mecanismo de las endorfinas en el dolor. También se acepta generalmente que la estimulación eléctrica interfiere de alguna manera en la conducción de los impulsos del dolor que van de la periferia del cuerpo hacia el cerebro. La teoría de Melzak y Wall sostiene que la estimulación de las fibras de mayor diámetro en los nervios sensoriales cierra un portón en el cordón espinal y esto interfiere con la transmisión de las señales de dolor al cerebro que son conducidas a través de las fibras de diámetro pequeño. La verdad es que necesitamos mas estudios científicos para determinar todo ésto.

### Estudios Experimentales

Ultimamente se han hecho estudios experimentales que nos pueden ayudar a mejorar nuestra manera de usar esta modalidad y que resultan un tanto interesantes:

1. *Localización del Tratamiento:* Noterman<sup>9</sup> evaluó el efecto de la estimulación eléctrica en voluntarios normales a los que le produjo dolor en los dientes aplicando una corriente de determinada intensidad en la pulpa del diente. Procedió entonces a evaluar los efectos del EGS (electro galvanic stimulator) estimulando en diferentes sitios. Encontró que el localizar los electrodos simultáneamente en la mejilla y en el punto de acupuntura Ho Ku, los sujetos experimentaron aumento en la tolerancia o el dintel del dolor. También se

obtuvieron los mismos resultados cuando estimuló la mejilla solamente. Sin embargo al estimular el Ho Ku solamente el efecto, fue insignificante. Esto nos prueba que la localización segmental del electrodo es la más efectiva en el tratamiento del dolor. Esto prueba también que el mecanismo por el cuál se alivia el dolor de esta manera es diferente al mecanismo que actúa en la acupuntura; en la que muchas veces el resultado es más efectivo cuando la aguja se introduce en un punto retirado del sitio del dolor.

2. *Intensidad del Tratamiento.* Se encontró que las intensidades bajas ayudaron muy poco al dolor. Sin embargo, cuando se usaron intensidades altas, suficientes para causar la contracción de los músculos faciales, hubo un aumento definitivo en el dintel del dolor. Podemos de nuevo inferir que esto se debe al aumento en la endorfina encontrado por varios investigadores.<sup>10</sup>

3. *Frecuencia de las Corrientes.* Se encontró que con el uso de frecuencias bajas, digamos de menos de 10 por segundo, el aumento que se produjo en el dintel del dolor fue gradual comparado con el obtenido con las frecuencias altas de 100 por segundo que fue inmediato.

Estos efectos se pudieron bloquear con naloxone (Narcan) que entendemos interfiere con la acción de las endorfinas. Las frecuencias altas dieron mejor resultado en los dolores agudos y las bajas en los dolores crónicos en estudios realizados por Herman.<sup>7</sup> De manera que todos estos factores de los que hemos hablado hay que considerarlos cuando usemos esta modalidad si es que queremos obtener resultados óptimos. Tampoco debemos olvidarnos de todos los otros factores que operan en los mecanismos que tienen que ver con la producción de dolor, especialmente en los casos de dolor crónico en los que tenemos un factor psicológico de gran importancia.

En resumen, podemos decir que las indicaciones para el uso de corrientes de alto voltaje y otras corrientes eléctricas han aumentado rápidamente en estos últimos años. Esto se debe a nuevos descubrimientos en la instrumentación y también a los hallazgos producidos en los últimos estudios científicos controlados que nos empiezan a delinear los mecanismos y a documentar los resultados. Sin embargo, todavía nos hace falta más información científica si es que la popularidad de esa modalidad se va a mantener.

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# Presentación de Casos

## Idiopathic Benign Recurrent Cholestasis in Second Cousins

Aurea I. Muñoz, M.D.  
Fermín Miranda, M.D.  
Ada Díaz de Silva, M.D.  
Juan Velázquez, M.D.

**I**diopathic benign recurrent cholestasis, a rare disorder of uncertain etiology, was first described by Summer-skil and Walshe in 1959.<sup>1</sup> Although the majority of reported cases have had onset of symptoms in childhood and adolescence, only a few patients of pediatric age have been described to date.<sup>2,3</sup> There are three sets of brothers among the affected patients,<sup>4,5</sup> but there is usually no family history of jaundice, and thus the evidence for a genetic defect is not conclusive. We now report the findings in two second cousins with this condition, each in turn born of consanguineous parents.

**Patient 1-** This 14 yr-old girl, the daughter of first cousins, had a recurrent pruritic condition diagnosed as atopic dermatitis since age 3 months. She also had frequent diarrheal episodes during infancy. At age 3 she had an exacerbation of pruritus, followed days later by jaundice, epigastric pain, and vomiting. The urine became dark and the stools light-colored. There had been no fever or exposure to hepatotoxins. There was no family history of jaundice or liver disease. On physical examination she was well developed and nourished, with moderate icterus and intense pruritus. The skin presented several excoriations. The liver edge was felt 3 cm below the RCM and was nontender. There were no other significant findings.

Routine laboratory investigations were nonrevealing, as were tests for various metabolic and infectious diseases. See Table 1 for results of representative liver function tests.

An operative cholangiogram revealed a normal excretory biliary system. Liver biopsy showed moderate to marked cholestasis in the canaliculi; the periportal spaces were slightly widened, with mild ductal proliferation and round cell infiltration. Occasional inflammatory cells were seen in the parenchyma. The findings were interpreted as consistent with a

prolonged cholangitic phase of hepatitis. Jaundice gradually subsided over a four-month period. The patient remained well until age 6, when she again became icteric after several days of intense pruritus. Physical and laboratory findings were similar to those on first admission. Open liver biopsy performed after subsidence of icterus revealed essentially normal findings were similar to those on first admission. Open liver biopsy performed after subsidence of icterus revealed essentially normal findings. Similar but milder episodes have recurred at intervals varying from a few months to several years. Cholestyramine, phenobarbital and antihistaminics have brought variable relief of pruritus. A cholecystectomy was performed at age 10 because of cholelithiasis. Liver function remains unimpaired between attacks.

**Patient 2-** A 2 1/2 yr-old girl, second cousin of Patient 1, was born of first cousins at term, weighing 2.8 kg. She had frequent hospitalizations for gastroenteritis since early infancy. At age 15 months she developed a pruritic rash followed days later by obstructive jaundice. Repeated questioning disclosed no family history of liver disease or icterus. Physical examination revealed an undernourished, markedly icteric infant with severe pruritus. The liver edge was palpable 6 cm below the RCM. Routine laboratory findings were unremarkable. Investigations for metabolic and infectious diseases, including hepatitis B, were nonrevealing. A sweat chloride determination was 14 meq/l. Results of representative liver function tests are shown in Table 1. Hepatobiliary <sup>99m</sup>Tc-IDA imaging showed an obstructive pattern. An operative cholangiogram was normal. Liver Biopsy revealed cholestasis, mainly as plugs in canaliculi, of predominantly centrilobular distribution; there were occasional inflammatory cells within the parenchyma (Figure 1). Several days postoperatively

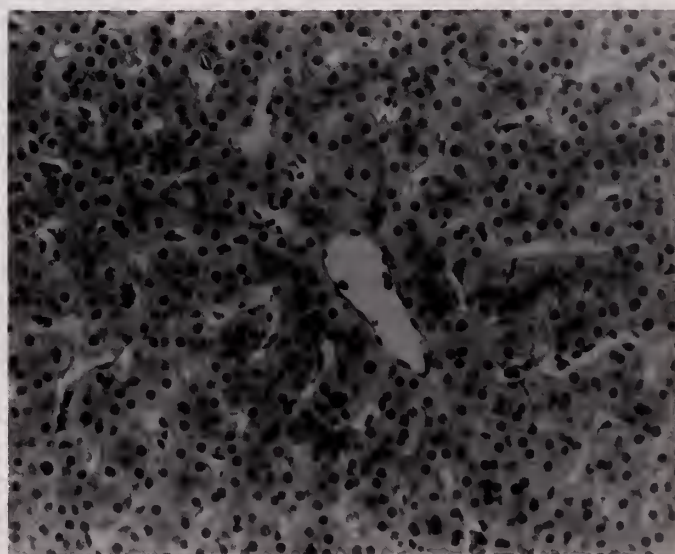


Figure 1. Biopsy of liver in Patient 2 showing a centrilobular area with bile plugs in canaliculi and occasional focal inflammatory cells. Normal arrangement of hepatic cell columns. (Hematoxylin and eosin; x 200).

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TABLE I

Results of Liver Function Tests*							
Episode of Jaundice	Serum Bilirubin (mg/dl) T/C	Serum AP U/L (nl 30-115)	SGOT/SGPT (U/L)	Serum Cholesterol (mg/dl)	Prothrombin Time (% normal)	Serum Proteins** (gm/dl) A/G	Serum Bile Acids (microgm/dl) (RIA-nl<68)
Patient 1							
1st episode	15.6/10.2	over 192	60/42	137	78	4.3/4.2	
2nd episode	4.6/2.3	over 400	150/26	—	82	3.9/3.6	7562
Patient 2							
1st episode	26.4/15.5	over 400	95/34	269	28	4.1/3.5	8000
2nd episode	22.4/15.9	over 350	122/--	166	69	4.2/2.6	

\* Abbreviations used: AP, alkaline phosphatase; T/C, Total / Conjugated; A/G, Albumin / Globulin.

\*\* Electrophoresis was done in all instances. Values within normal range except for slightly elevated beta-globulin in Patient 2.

the patient's relationship to Patient 1 became known to us and the correct diagnosis was entertained. A three-week course of prednisone was administered and icterus gradually resolved five months after onset. At age 26 months the patient had a second cholestatic episode. Physical and laboratory findings (see Table 1) were similar to those on first admission, except that the nutritional state was now improved. Treatment included antihistaminics and a topical skin lotion. Icterus lasted six weeks, the liver profile being normal thereafter.

### Discussion

Clinical and laboratory features as described are characteristic of benign recurrent intrahepatic cholestasis. Itching, invariably the first symptom and generally quite troublesome, antedates jaundice for variable periods, at times for years. Weight loss and steatorrhea are additional manifestations. Nausea, abdominal pain and hepatomegaly may occur. The frequency and duration of the attacks vary considerably, even in individual patients.

Liver function tests characteristically show cholestatic features. Increases in serum bilirubin, predominantly the conjugated fraction, to values as high as 40 mg/dl have been reported.<sup>1</sup> Serum alkaline phosphatase and bile acids are significantly elevated. Serum cholesterol, transaminases, and alpha - 2 and beta-globulins may be moderately increased. The liver profile returns to normal during remissions.

Liver biopsy findings by light microscopy are as described in our patients, and revert to normal between episodes, as in Patient 1. Electron microscopy reveals dilatation of bile canaliculi, with blunting of the microvilli of the canalicular membrane. Numerous vesicles containing a nonlipid material are present intracellularly.<sup>6</sup>

The pathogenesis is obscure; the fact that serum bile acids rise before the onset of jaundice suggests and underlying defect of bile acid metabolism. The ultramicroscopic liver findings, similar to those seen after norethandrolone administration,<sup>7</sup> might account for the formation of bile with abnormal physicochemical properties, predisposing to stasis, canalicular dilatation and further membrane damage.<sup>8</sup>

Other types of familial conjugated hyperbilirubinemia considered in our patients include the Dubin-Johnson and Rotor Syndromes. In these conditions, however, bile salt excretion is normal, pruritus is absent, and liver biopsy shows

no cholestasis. Intrahepatic biliary hypoplasia syndromes such as Byler disease and a recently described form of familial cholestasis with elevated sweat electrolytes,<sup>9</sup> also manifest early onset of fluctuating jaundice, pruritus and malabsorption. The clinical course, however, is progressive, and liver histology shows hypoplasia of bile ductules and increased fibrous tissue. Parenthetically, Patient 2 had a normal sweat chloride concentration. Metabolic conditions such as galactosemia, hereditary tyrosinemia, and alpha 1 - antitrypsin deficiency were excluded on clinical grounds and by appropriate laboratory investigations.

Treatment of this condition is supportive. Deficiencies of fat-soluble vitamins, if present, are corrected. Cholestyramine, antihistaminics and phenobarbital have been employed for relief of pruritus. Corticosteroids in patients with prolonged jaundice have given variable results.

The present report provides further evidence for the genetic transmission of this disorder and underscores the importance of obtaining a reliable family history on patients with jaundice. An early awareness on our part of the patients' consanguinity would have greatly simplified the diagnostic approach to Patient 2.

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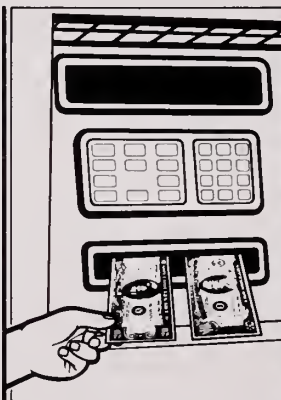
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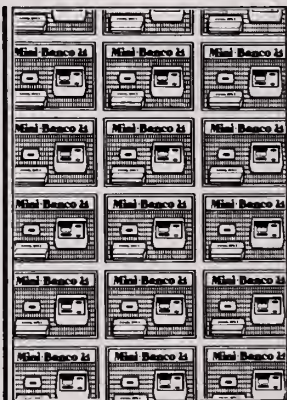
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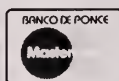
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# ARTICULOS ESPECIALES

## Uso de Psicofármacos por el Médico Primario Principios Generales

J.A. Nuñez-López, M.D.\*

La necesidad de recibir y reaccionar a estímulos variados y la capacidad de sentir dolor son dos de las características del ser humano asociadas a su supervivencia que le han hecho vulnerable al uso y abuso de sustancias químicas.

Los psicofármacos son sustancias químicas que alivian el dolor psíquico, alteran el estado de ánimo e indirectamente la forma de pensar de todas las personas que los utilicen. Han sido de gran utilidad y han aliviado el dolor social de nuestra comunidad.

Estas sustancias afectan directamente lo que uno es. Trabajan sobre el órgano que controla todos nuestros sentimientos, pensamientos y actuaciones. Modifican nuestra forma de sentir, nuestra forma de pensar y por ende nuestra conducta. Está probado que reducen irritabilidad, respuestas a estímulos de dolor, inducen el sueño y producen cambios en los estados de ánimo.

Toda sustancia que ayuda a evadir dolor conlleva el riesgo que se utilice inapropiadamente. El hombre ha trabajado siempre para evitar la muerte, y el dolor ha sido siempre un indicador de peligro, de riesgo de muerte. Sin embargo, el dolor psíquico y/o físico son esenciales para movernos a actuar, a decidir, a cambiar, a corregir, a crear. El riesgo del abuso o uso inapropiado a nivel individual es pequeño al lado del riesgo a nivel de pueblo. Y somos nosotros los médicos, dentro de una multiplicidad de factores los que más directamente podemos decidir sobre el uso de estas sustancias.

### Uso y Abuso

El uso inadecuado (abuso) de los psicofármacos comenzaron junto al uso apropiado aproximadamente desde el 1954. Se comenzaron a utilizar con psicóticos. Su impacto fue la reducción del uso de los hospitales psiquiátricos. Se pudieron evitar admisiones y readmisiones. Se ayudó a reducir la incapacidad del paciente psicótico en su vida familiar, social y ocupacional. Junto con los beneficios, vinieron las complicaciones del uso. Ejemplo, dosis excesiva que prolongaban la hospitalización al encubrir otras condiciones como las depresiones. Inclusive, se podían utilizar para el bienestar de empleados y no de pacientes. El uso más generalizado en Puerto Rico comenzó desde el punto de vista gubernamental, en el año 1967 cuando se iniciaron los centros de salud mental. Se amplió el uso apropiado. Se evitaron muchas crisis familiares, se evitó pérdida de trabajo, pérdida de estudio. Al aliviar a maestros se mejoró la condición de estudiantes, al mejorar padres se abrió un mejor futuro a los hijos.

Cuando se generaliza el uso de una sustancia hay más oportunidades también para el uso inapropiado, en particular cuando se utilizan sustancias que puedan llegar a más población. Ejemplo, los tranquilizantes menores, los psicofármacos que se utilizan para el paciente no-psicótico. Más personas, con más distintos propósitos comenzaron a utilizarlos. En los años sesenta los psicofármacos fueron una de las sustancias más utilizadas por la juventud en grandes dosis. Actualmente los tranquilizantes menores son una de las sustancias más recetadas por el médico primario.

### Principios Generales para Evitar el Uso Inadecuado

¿Qué puede hacer el médico primario para evitar contribuir al uso inadecuado de los psicofármacos?

1. Primero debe *conocer bien unos pocos medicamentos de utilizad para las condiciones psiquiátricas que más comunemente el va a atender*. No se debe abrumar por la cantidad grande de psicofármacos que existen ni tampoco debe tratar de probar todo aquel fármaco nuevo que viene al mercado. Realmente en los últimos años han sido muy pocas las sustancias que tienen ventajas significativas sobre otras. Es mucho más conveniente conocer bien un grupo pequeño de antipsicóticos y antineuróticos que tener un conocimiento superficial e inadecuado de gran número de ellos.

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2. *Es necesario hacer un diagnóstico correcto.* Si usted se equivoca de diagnóstico va a terminar usando un medicamento que no va a ser efectivo para la condición. Ejemplo, en el caso de psicosis si utiliza antineuróticos el paciente va a tender a consumir grandes cantidades para conseguir alivio, lo cual aumentaría el riesgo de efectos secundarios y de una dependencia excesiva a estos medicamentos.
3. *Es esencial que e tomen unos minutos para explicarle el uso y los efectos secundarios de medicamentos al paciente y al familiar.* Esto evita expectativas exageradas de ambos, con el consecuente cambio prematuro de un tranquilizante a otro o peor de un antidepresivo a un tranquilizante, lo que puede traer complicaciones en el tratamiento y el uso innecesario prolongado de medicamentos que no son efectivos para la condición del paciente.
4. *Haga un plan de tratamiento y déjeselo saber al paciente o al familiar,* esto evitará el uso irregular de los mismos, consumo de dosis inadecuadas y facilitará el consumo de dichos medicamentos por un tiempo limitado.
5. *Determinar el momento de referir a un especialista.* Si después de una prueba con medicamentos y ayuda de entrevistas cortas el paciente no mejora o empeora debe ser referido a un especialista y evitar el seguir aumentando dosis o cambiando de un medicamento a otro. Estos cambios fomentan dependencia a los mismos y fortalecen la relación condición emocional y medicamento, vis-a-vis condición emocional y brega con problemas de tipo psicosocial.
6. *Tratar de identificar a tiempo cuando el medicamento se está usando para evadir la solución de un problema.* Ejemplo, la esposa que consume medicamentos en dosis altas durante la noche y así evitar el contacto íntimo con su esposo a aquella que al utilizarlos llena en forma exagerada sus necesidades de dependencia.

Posiblemente, hay un número mínimo de casos que al tener una baja tolerancia al dolor psíquico de tipo congénito requiere el uso ocasional de estos medicamentos por tiempo indefinido. Aún así, en estos casos el médico podría ayudar en términos de fortalecer la capacidad del paciente para bregar más eficientemente con problemas del diario vivir y así evitar conflictos y situaciones que produzcan dolor psíquico en el cliente y le precipite la necesidad del uso de medicamentos.

Los médicos están en una posición ideal para evitar el uso inadecuado de estas sustancias y al fomentar el uso apropiado reducir significativamente todas las complicaciones psicosociales que surgen por no haber manejado a tiempo, una condición de origen emocional en sus pacientes.

### Clasificación Funcional de Psicofármacos

Como hemos mencionado, los psicofármacos son sustancias químicas que al modificar el estado de ánimo, el nivel de ansiedad, los problemas de percepción y pensamiento asociado a condiciones emocionales, facilitan la recuperación del paciente que sufre de dichas condiciones.

Los psicofármacos se pueden clasificar como antineuróticos, antisicóticos y antidepresivos tomando como base las condiciones con las cuales son más efectivos.

Bajo antineurótico tenemos una serie de medicamentos cuyo efecto primordial es la reducción del nivel de ansiedad.

Podemos mencionar bajo esta clasificación los medicamentos bien conocidos como lo son *Valium, Librium, Serax, Vistaril* y entre los recientes, *Ativan, Tranxene, Paxipan, Xanax* y *Centrax*.

Los antipsicóticos son aquellos que son efectivos en reducir la sintomatología del paciente psicótico que tiene que ver con disturbios de percepción y pensamiento como lo son alucinaciones y delirios. Los más conocidos son el *Thorazine, Mellaril, Stelazine, Compazine, Trilafon* y *Haldol*. Algunos de menos uso pero con indicaciones específicas; como el *Prolixine* intramuscular y otros más recientes; como lo son el *Serentil, Navane, Moban, Loxitane* y *Lidone*.

Bajo antidepresivos clasificamos aquellos que son efectivos en reducir la sintomatología depresiva y podemos mencionar los más conocidos como *Tofranil, Elavil, Norpramin* y entre los recientes *Sinequan, Surmontil, Ludiomil, Asendin* y *Desyrel*.

Las casas farmacéuticas han producido combinaciones de medicamentos pero no aconsejamos el uso de los mismos ya que es preferible utilizar los medicamentos por separados, lo cual nos permite identificar los efectos de cada uno y regular mejor las dosis a tono con la condición, según la respuesta del paciente.

Hay un medicamento exclusivo para la psicosis maniaco-depresiva que es más bien el uso del psiquiatra, *Carbonato de Litio*. Tenemos medicamentos asociados al uso de tranquilizantes y antidepresivos como lo son los antiparkinsonianos siendo los más utilizados, *Congentin* y *Artane*.

Hay medicamentos que podemos llamarlos anti-insómnicos, ya que no son hipnóticos clásicos, sin embargo, inducen el sueño. Muchos psiquiatras prefieren bregar con la sintomatología que está detrás de la pérdida de sueño y no arriesgarse al posible abuso de anti-insómnicos.

### Algunas Recomendaciones Generales Sobre el Uso de Antipsicóticos, Antineuróticos y Antidepresivos

Como habíamos aclarado inicialmente una de las formas de evitar complicaciones en el uso de medicamentos es explicarle al paciente lo que está tomando. Obviamente, el explicarle a un paciente que se le va a recetar un antineurótico conlleva, explícitamente, el confrontarlo con la realidad de que sus síntomas están provocados por conflictos sin resolver en algunas de las áreas de su funcionamiento psicosocial. El solo hecho de confrontar al paciente con que posiblemente problemas de carácter psicosocial, le estén afectando en una medida que le produzcan síntomas en su cuerpo, muchas veces moviliza muchísimos recursos internos y familiares que ayudan a bregar con el problema.

Se le debe preguntar sobre los medicamentos que esté utilizando el paciente y así evitar combinaciones innecesarias de psicofármacos. Al iniciar un paciente en psicofármacos debe dársele solamente cantidad suficiente por un corto período de tiempo, no más de una semana. En su segunda visita se debe explorar primero si el paciente está tomando el medicamento. Esto debería hacerse con un tono de voz y una actitud que permita al paciente ser sincero con el médico.

En caso de que se utilicen antidepresivos, se le debe hacer claro al paciente y al familiar que no se esperen efectos dramáticos por las primeras dos (2) o tres (3) semanas. Esto evita que el paciente prematuramente descontinúe el tratamiento, innecesariamente visite otros colegas que tendrán que comenzar nuevamente con todo el proceso de diagnóstico y tratamiento.



Si se utilizan antipsicóticos se le debe aclarar a los familiares los efectos secundarios. En particular, la akathisia que hace que el paciente se mueva, aparentemente, intranquilo de un sitio a otro y siente que mientras está acostado los pies se le mueven solos. Con frecuencia los pacientes y/o sus familiares deciden aumentar la dosis porque interpretan están más ansiosos, complicando el cuadro de reacción secundaria. Así mismo, se le debería explicar al familiar de que un efecto secundario podría ser una condición no peligrosa pero sí que asusta, como lo son espasmos de los músculos del cuello, de la boca y de los músculos del ojo.

En muchas ocasiones el no explicarle este posible efecto secundario ha hecho que el paciente termine en un centro médico con evaluaciones neurológicas e inclusive hospitalización para luego descubrir que estaba tomando un antipsicótico.

Una de las preguntas más importantes al paciente que necesita un medicamento tranquilizante es, "cuál de los tranquilizantes que has tomado en tu vida es el mejor que te ha caído para la sintomatología que tienes al presente". Con frecuencia el paciente y los familiares saben cuál es el mejor medicamento y el médico en este caso debería dejarse llevar por la experiencia de ellos.

Ayuda mucho al paciente y a su familia el que se haga claro que el medicamento sólo ayuda reduciendo los síntomas de la condición, pero que está en el paciente y en su familia el recurso principal. La reducción de sus síntomas va a depender de cómo el bregará con las situaciones que a él le están afectando, causándole ansiedad, depresión, produciéndole una recaída de su condición psicótica. En ocasiones hay que explicar que entrevistas cortas dirigidas a ayudar al paciente, acompañada por dosis bajas de medicamentos; pueden ser más efectivas que altas dosis de medicamentos sin bregar con los problemas que están perpetuando la condición del paciente.

Esta explicación aumenta las posibilidades de que el paciente que le llega tomando varios psicofármacos o dosis relativamente altas le acepte bajar las dosis y reducir los medicamentos a un mínimo.

Con frecuencia pacientes con síntomas secundarios asociados a "stress" como insomnio, anorexia y cansancio responden a entrevistas cortas en las cuales se focalice sobre agentes precipitantes y se ayude en el manejo de las mismas. De no poder ofrecer esta ayuda el médico debe referir el caso antes de tratar de sustituir la misma con el uso de psicofármacos.

### Recomendaciones Generales sobre Dosificación

Una vez el médico decide utilizar el psicofármaco uno de los factores que más determina el uso efectivo del mismo, es la dosificación. Este factor cobra importancia en el caso del paciente psicótico agudo al cual se le puede evitar la hospitalización de veinticuatro horas si se utilizan dosis adecuadas de antipsicóticos. Ejemplo, el paciente que viene a la consulta agitado con extrema ansiedad, alucinaciones, delirios y con historial de no haber dormido durante los últimos días, con frecuencia requiere el uso de un antipsicótico intramuscular (*Thorazine*, 100mgs) cada seis u ocho horas por tres o cuatro dosis. Algunos psiquiatras han comenzado a utilizar *Haldol* intramuscular en dosis repetidas a cortos intervalos para lograr la sensación óptima en tres o cuatro horas. Luego se puede cambiar la medicación por vía oral, ejemplo, *Mellaril* 200 mgs, tres veces al día.

Después de este manejo inmediato, que en algunas ocasiones tendrá que hacer el médico primario sin la consultoría del especialista podría referir el paciente en una condición más controlada al psiquiatra o continuarlo en tratamiento en el caso de que sea un paciente de esquizofrenia crónica conocido por el médico.

El paciente psicótico crónico a veces requiere dosis altas por tiempo indefinido. Es importante que el médico no reduzca dramáticamente la dosis porque vea al paciente funcionando aparentemente bien. De decidir bajarla debe aumentar la frecuencia de visitas idealmente a una por semana. Deberá hacerle claro al paciente y sus familiares de que en caso de que desarrolle alguno de los síntomas anteriores se le podrá subir la dosis sin problema alguno. Inclusive, el paciente que ya conoce bien los síntomas de su enfermedad se le puede dar libertad para tomar medicación entre un mínimo y un máximo dependiendo de cómo él evalúe su propia condición.

Los pacientes psicóticos agudos se deben mantener en dosis altas de medicamentos mientras exhiban síntomas psicóticos. Idealmente, después de la desaparición de los mismos, debería mantenerse la dosis por dos a cuatro semanas para luego ir reduciéndola gradualmente, ejemplo, de 50 a 100 mg cada dos semanas.

El paciente con una condición de ansiedad aguda severa a veces requiere una primera dosis de antineurótico intramuscular, lo cual se puede evitar si hay tiempo para establecer una relación con el paciente y desarrollar un plan de ayuda a través de los familiares. Usualmente, este paciente se debe comenzar en niveles altos de antineuróticos, ejemplo, *Librium* 25 mgs cuatro veces al día, *Valium* 10 mg cuatro veces al día o *Ativan* 2 mg tres veces al día. En ocasiones, el usar esas dosis permite que el paciente regrese a su trabajo en dos o tres días evitando complicaciones en el área ocupacional que generan por sí, ansiedad y tienden a perpetuar el cuadro.

La dificultad mayor de mantener un paciente neurótico inicialmente en dosis adecuada de medicamento es con aquel que tiene temor a la dependencia del medicamento y se considera muy autosuficiente. En este caso hay que aclarar que el uso será por un tiempo limitado y que se le irá reduciendo rápidamente según lo permita su condición. De observarse que el paciente aumenta la dosificación por su propia cuenta se debería considerar que el diagnóstico no es el correcto y referir para consultoría o tratamiento al especialista.

El paciente con un disturbio depresivo mayor que se decide medicar con antidepresivo usualmente se debe comenzar con una dosis de entre 75 a 100 mgs. por día dividida en dos o tres dosis al día y una mayor antes de acostarse. Se podría ir aumentando si se considera necesario la dosis hasta niveles de 150 a 200 mgs diarios en un término de dos a tres semanas. En ocasiones el paciente con síntomas depresivos asociados a disturbio de ajuste o episodios depresivos mayores con síntomas psicóticos responden a una combinación de entrevistas cortas de quince a veinticinco minutos semanales y el uso de antidepresivos (*Amitriptilina*) en dosis de 25 a 50 mgs antes de acostarse.

El paciente con un episodio depresivo mayor y síntomas psicóticos requiere combinar un antidepresivo con un antipsicótico. Posibles combinaciones son; por ejemplo: comenzar con antidepresivos 50 mgs al acostarse y 25 mgs dos veces al día junto a antipsicóticos que vienen en dosificaciones de 1 a 10 mgs. (*Stelazine*, *Haldol*).

La dosis de antidepresivos y antipsicóticos se deben modificar a intervalos semanales dependiendo del desarrollo del

caso. Usualmente, hay que subir a dosis de 150 a 200 mgs, diarios de antidepressivos y antipsicóticos a dosis de 150 a 300 mgs diarios o su equivalente en antipsicóticos que vienen en dosificaciones de 1 a 10 mgs. La utilización de estos medicamentos más allá del manejo inicial usualmente requiere la intervención del psiquiatra.

El paciente depresivo psicótico y su familia deben saber el tratamiento de psicofármacos se puede extender de seis meses a un año y que pueden ocurrir recaídas según se le va reduciendo la dosis.

Algunos antidepressivos como *Doxepin* y *Elavil* producen somnolencia en muchos pacientes. Se les debe explicar posiblemente les de mucho sueño los primeros tres o cuatro días, pero luego este efecto se reduce. De ser muy marcado el efecto sedante se debe concentrar la dosificación mayor a la hora de acostarse, antes de considerar cambiar a otro antidepressivo.

### Complicaciones y Efectos Secundarios del Uso y Abuso de Psicofármacos

Las complicaciones de mayor costo social son las menos visibles. Realmente, no sabemos cuántas personas al caer en una crisis de un ajuste psicosocial en vez de analizar y re-evaluar su situación para determinar alternativas de manejo optan por utilizar irregular e indefinidamente psicofármacos. El utilizar medicación que controla los síntomas, le reduce la motivación para introducir cambios en su estilo de vida y le perpetúan un estado de stress parcialmente reducidos con medicamentos que le hace vulnerable a sufrir crisis mayores.

Igualmente, no tenemos información hasta dónde los psicofármacos interactuando con otros medicamentos y drogas; en particular, el alcohol y utilizados sin prescripción médica contribuyen a muertes o incapacidad por accidentes del trabajo, de automóviles y por complicaciones cardíacas.

Estas dos complicaciones hacen imperativo que el médico primario enfatice la seriedad que conlleva el ingerir una sustancia que actúa sobre nuestro cerebro, donde reside el control de nuestras funciones vitales.

El efecto secundario más frecuente asociado al uso de antineuróticos es somnolencia, cuando se usan los medicamentos en su dosificación mayor. Usualmente, este efecto secundario se puede utilizar positivamente, pues le permite al paciente que sufre de ansiedad severa descansar por dos o tres días. El paciente que desea regresar en un corto período de tiempo a su trabajo se le puede reducir o eliminar la dosis de la mañana y/o del medio día, según necesario.

Los antipsicóticos producen ocasionalmente cuadro de akathisia y/o diskinesia. Estos se controlan con relativa facilidad bajando la dosis y dando por tres o cuatro días de antiparkinsoniano como *Artane* o *Congentin*.

Efectos de tipo anticolinérgicos son frecuentes en un nivel tolerable para el paciente y se reducen a los varios días sin requerir manejo sintomático. Ocasionalmente los síntomas son tan molestos que hacen necesario cambiar el medicamento.

La somnolencia secundaria a Amitriptilina (*Elavil*), usualmente se reduce luego de dos a tres días. De continuar, se debe concentrar la dosis mayor antes de acostarse.

La complicación más peligrosa secundaria al uso de antidepressivos tricíclicos (*Elavil*) son las arritmias cardíacas. En caso de dudas sobre la susceptibilidad del paciente, éste debe evaluarse físicamente antes de decidir la medicación y dosis a ofrecerse.

Cuando se recomienda antipsicóticos por vía intramuscular y ocasionalmente por vía oral hay que adelantar o informar al paciente y sus familiares sobre la posibilidad de mareos secundarios a hipotensión postural. Con frecuencia basta evitar cambios súbitos de posición para evitar los mareos y/o colapsos.

El inicio de somnolencia en un paciente psicótico después de varios días de tratamiento con antipsicóticos, a veces indica una menor tolerancia de los medicamentos según se mejora de la sintomatología aguda y se puede tomar como inicio de que se puede iniciar la reducción gradual de medicamentos.

Los efectos secundarios se reducen al utilizarse las dosis adecuadas de los medicamentos indicados. La tolerancia a dichos efectos aumenta cuando el paciente y su familia se mantienen bien informados sobre la gran variedad de reacciones a nivel individual y tienen claro la necesidad de contar con un plan de tratamiento flexible durante las primeras visitas.

### Conclusión

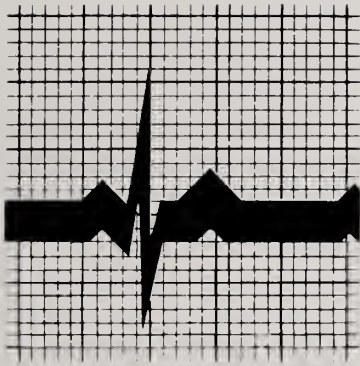
Los psicofármacos facilitan el manejo integral del paciente por los médicos primarios. Al afectar el funcionamiento del cerebro, órgano que integra los ambientes internos y externos convierte a estos, en los medicamentos con más potencial de afectar la forma de ser del paciente y por ende, su estilo de vida.

Su uso apropiado dependerá siempre de que el médico primario nunca olvide la seriedad envuelta en el hecho de ofrecer una sustancia que afecta en la forma más amplia los sentimientos, pensamientos y la conducta del ser humano y por ende los peligros que conlleva olvidar su potencial para cambiar la vida misma de sus pacientes.

Se han utilizado nombres comerciales de algunos psicofármacos para facilitar la identificación de los mismos por el médico primario. El autor no favorece el uso de unos medicamentos sobre otros de composición química similar. Se recomienda el médico primario debe tener en su biblioteca de referencia inmediata libros que incluyan la clasificación de los psicofármacos, el manejo inmediato de intoxicación por el uso de los mismos y la interacción de estos con otros medicamentos. Debe familiarizarse por lo menos con un medicamento de las clases más utilizadas. A continuación ejemplo de algunos textos que se recomiendan para uso práctico del médico general.

1. *Psychiatry in General Medical Practice*  
Gene Usdin, M.D., Jerry M. Lewis, M.D., McGraw-Hill Book Company.
2. *Psychiatry for the Primary Care Physician*  
Arthur M. Freeman, III, MD, Robert L. Sack, MD and Philip A. Berger, MD, The Williams & Wilkins Co. 248- E. Preston St. Baltimore, Maryland.
3. *The Practicing Physician's Approach to Headache*  
Second Edition, Seymour Diamond, MD and Donald J. Dalesio, MD
4. *Behavioral Medicine, Theory and Practice*  
Edited by Ovide F. Pomerleau, PhD and John Paul Brady, MD.
5. *Clinical Psychiatry in Primary Care*  
Steven I. Dubovsky, MD and Michael p. Weissberg, MD
6. *Understanding Human Behavior in Health and Illness*  
Richard C. Simmons, MD. Herbert Pardes, MD.
7. *Psychotropic Drugs: Emergency Manual*  
Second Edition, Nathan S. Kline, MD, FACP. Jean Pierre Lindenmayer, MD.
8. *Drug Interactions Index*  
Fred Lerman, MD. Robert T. Weibert, Pharm. D.





# ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD

This 48-year-old male with adult-onset Type 1 diabetes mellitus was admitted to the hospital on 3-9-82, with sore throat, dizziness, vomiting, fever, a foot ulcer, epigastric and left chest pain. There were numerous previous hospitalizations for uncontrolled diabetes. He was taking NPH insulin, and methyldopa for hypertension. The blood pressure was 140/100 mm Hg. Laboratory data were as follows: WBC 18,600 with 87 segmented cells and 9 stabs, blood sugar 750 and 900 mg/dl, small plasma acetone, 3 + glucose and 2 + ketones in the urine, cholesterol 143 mg/dl, BUN 31 mg/dl, serum sodium 130, chloride 90 and potassium (K) 5.8 and 9.4

(hemolyzed) meq/L;  $\text{CO}_2$  10 meq/L and  $\text{HCO}_3$  5 meq/L, pH 7.17, base excess -21; CVP 4 cm water; chest roentgenogram normal; the cardiac examination was normal. The electrocardiogram (ECG) is illustrated in Figure 1. The patient's dehydration and hyperglycemia were controlled with hydration and insulin.

## Questions

1. What is the diagnosis by ECG?
2. What is the pathogenesis of this pattern?

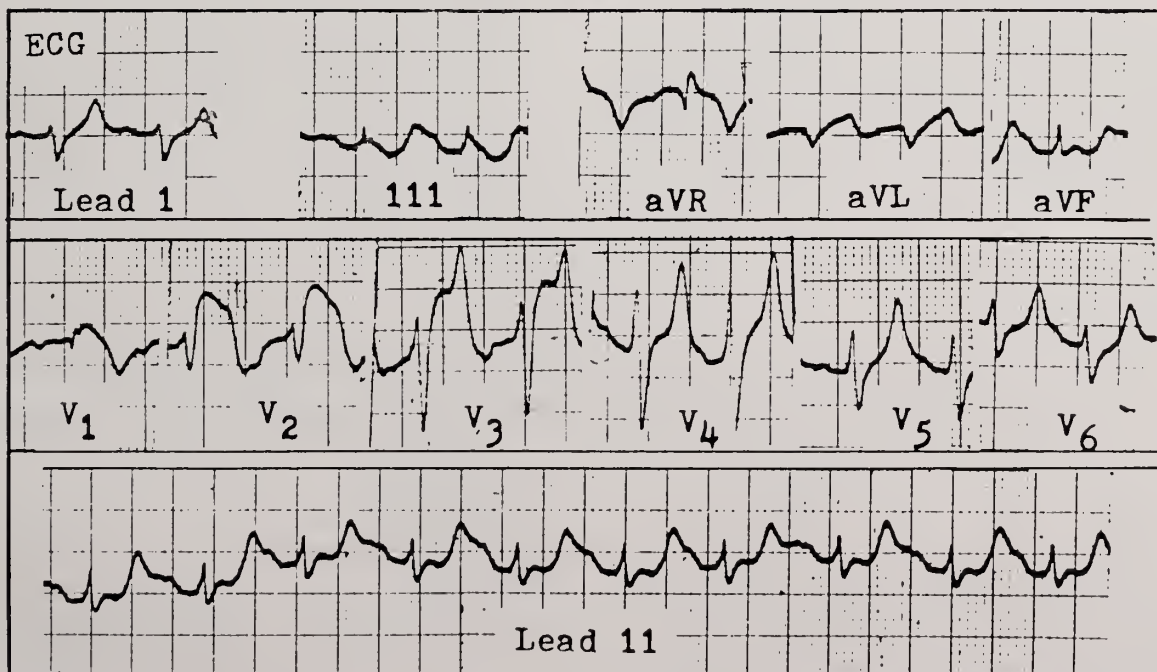


Figure 1

Answers

Pseudo-acute anteroseptal myocardial infarction (MI).

Figure 1 ECG (3-9-82) reveals sinus tachycardia, Q-T interval 0.33 S, right axis deviation, broadened QRS complexes with a right bundle branch block pattern and QS complex in aVL, peaked T waves and elevated convex ST segments in leads aVL, V<sub>1-3</sub>, suggesting an acute anteroseptal MI.

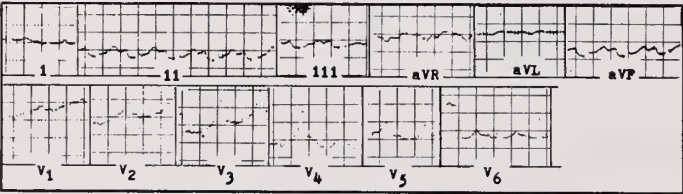


Figure 2

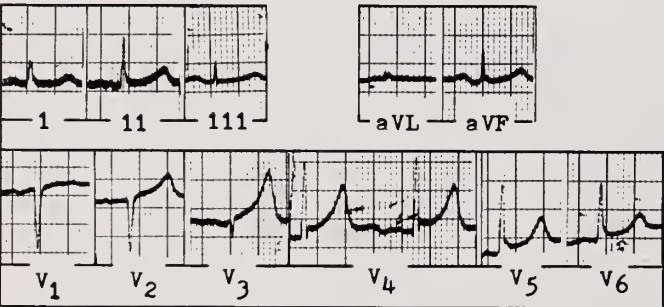


Figure 3

Within one-half hour after therapy the ECG had reverted to its basic status, Figure 2 (which photographs less well), similar to many previous ECGs, Figure 3 obtained over the prior 10 years. These traces showed poor r wave progression, but a increasing r/S ratio, from leads V<sub>1</sub> to V<sub>3</sub>, and concave ST segment elevation suggesting the early repolarization syndrome. The P-R segment may be depressed in leads II, III and aVF.

Serum enzymes were:

	SGOT(normal 7-40 u/L)	CPK (normal 50-325 u/L)	LDH (normal 100-225 u/L)	Creatinine
3-9-82	33	352	253	3.1 meq/L
3-10	42,37	540	244, 278	
3-10	—	—	—	
3-10	43	673	268	
3-13	21	190	118	

Comments

Hyperkalemia (K 8-10 meq/L) can rarely produce a pseudo-acute MI or acute pericarditis pattern on the ECG, by loss of R waves, transient Q and QS waves in V<sub>1-3</sub> or inferior leads, and “dialyzable injury currents” shown as coved ST segment elevations and T wave inversions.

The Q waves may be due to marked conduction impairment during ventricular septal depolarization, and the “Injury Current” to QRS widening and marked derangement in the K<sub>I</sub>/K<sub>E</sub> ratio, and nonhomogenous depolarization in different portions of the myocardium.

Hyperkalemia is often present in the untreated patient with diabetic acidosis on admission to the hospital, and hypokalemia ensues once therapy is initiated.

Recently, a similar case as this patient was reported, believed to be the first with this combination of hyperkalemia, diabetic acidosis, acute anteroseptal pseudomyocardial infarction and bifascicular block (Cohen A, Utarnachitt RV: Electrocardiographic changes in a patient with hyperkalemia and diabetic acidosis associated with acute anteroseptal pseudomyocardial infarction and bifascicular block. Angiology 32: 361, 1981).

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The patient had no subsequent chest pain, and has done well since.



## IN MEMORIAM

El día 3 de mayo de este año se cumplió el primer aniversario de la muerte del Dr. Félix M. Reyes. La ocasión se presta para recordar la obra de uno de nuestros primeros patólogos, obra poco conocida, ya que el Dr. Reyes nunca fue partidario ni de la publicidad ni de la ostentación. Su manera de ser, humilde y sencilla, la mantuvo, la mayor parte del tiempo, dentro del ámbito del laboratorio.

Pocos saben que el Dr. Reyes, después de recibir el título de Bachiller en Ciencias de la Universidad de Puerto Rico (1926), se graduó de médico en la Universidad de Columbia, Nueva York (1930). Después de hacer dos años de internado, continuó sus estudios en "City Hospital" y "Sea View Hospital", Nueva York, como residente en medicina interna. Año y medio más tarde regresó a Puerto Rico (1934) y empezó a trabajar en el Departamento de Salud en el campo de la tuberculosis. En julio de 1936, inició una residencia de tres años y medio en patología bajo la dirección del Dr. Enrique Koppisch en el hospital de la Escuela de Medicina Tropical.

A fines de 1939, el Dr. Reyes se convirtió en el *primer* Jefe del Departamento de Patología y Laboratorio Clínico del ya desaparecido Hospital de Distrito de Bayamón. Fue aquí donde le conocí. Yo había empezado mi internado en ese hospital a principios de 1943 y, aunque ya él se encontraba sirviendo en el ejército de los Estados Unidos, seguía viniendo, vestido de militar, al hospital a completar los expedientes de autopsias hechas por él.

Volví a tratar al Dr. Reyes en 1947 cuando, al licenciarse del ejército pasó a ser el *primer* Jefe del Servicio de Laboratorio Clínico del también desaparecido Hospital San Patricio (Veteranos). Aquí se dedicó principalmente a la patología anatómica (su campo favorito) y a la supervisión de la patología clínica. Más tarde, el Dr. Ramón Ruiz Nazario le asistió en el Laboratorio Clínico y el Dr. José E. Taveras en patología. El Dr. Gustavo Ramírez de Arellano sucedió al Dr. Taveras. El Dr. Reyes se jubiló poco antes de que el hospital se mudara a su nueva ubicación. El Dr. Ramírez de Arellano pasó a ser jefe del departamento.

El Dr. Reyes fue socio fundador de la Sociedad de Patólogos de Puerto Rico (1956). Después de haber ocupado el puesto de secretario-tesorero, fue elevado a la presidencia en 1958. En 1960, también fue electo presidente de la Sección de Patología de la Asociación Médica de Puerto Rico.

En cuanto a sus valores académicos se debe apuntar que el Dr. Reyes aprobó sus "Boards" en patología en 1946, fue nombrado Profesor Clínico Asociado de Patología en nuestra Escuela de Medicina y fue aceptado en prestigiosas asociaciones profesionales incluyendo el "College of American Pathologists". Publicó varios artículos de orden científico. Fui su co-autor en el que se informó por vez primera en Puerto Rico, un caso de rotura del músculo papilar secundario a un infarto del miocardio.<sup>1</sup>

En la primera asamblea de la Sociedad de Patólogos, el 25 de mayo de 1957, el Dr. Reyes presentó un caso de hepatoma y sugirió, antes que cualquier otro investigador, que una hipoglicemia co-existente parecía estar relacionada con el tumor



hepático. Posteriormente, aparecieron publicaciones en la literatura médica señalando dicha asociación.

El Dr. Reyes fue de los primeros en Puerto Rico en hacer estudios citológicos de secreciones para diagnosticar el cáncer y en 1959 fue el patólogo a cargo de la primera conferencia clínico-patológica llevada a cabo en una asamblea de la Asociación de Patólogos. En 1960, el Dr. Félix M. Reyes es incluido en un exclusivo grupo de patólogos en honor de los cuales se ofrece el Banquete Presidencial de la Asamblea Anual de la Sociedad de Patólogos "por sus contribuciones al desarrollo de la anatomía patológica y la patología clínica en nuestra Isla". Estas son las credenciales del patólogo.

Como persona, el Dr. Reyes fue siempre todo un caballero, gentil, bondadoso, servicial, siempre dispuesto a ir en la ayuda del compañero. De carácter tranquilo, lento caminar y de poco hablar, sin embargo, se distinguió como fiel cumplidor en su trabajo. Se tomaba su tiempo para rendir el informe de una autopsia, pero éste, una vez terminado, era el ejemplo de un informe completo, reultado de un estudio minucioso del caso. Su honradez intelectual y su intachable conducta profesional se significaron en 1957 cuando, durante las deliberaciones de la segunda reunión anual de la Sociedad de Patólogos, a moción de él, se creó el Comité de Ética de dicha entidad.

Es obvio que el Dr. Félix M. Reyes fue durante toda su vida profesional un médico en todo el sentido del vocablo. No se podrá escribir la historia de la patología en Puerto Rico sin incluir su nombre.

1. Reyes, Félix M., Torres, José M.: Rupture of a Papillary Muscle in Myocardial Infarction. Bol Asoc Med P Rico 1967; 59:196.

## **DR. COLLINS ISN'T PAYING HIS MALPRACTICE INSURANCE PREMIUM THIS YEAR.**

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# Resúmenes de La Literatura Médica



**PERIPHERAL NERVOUS SYSTEM COMPLICATIONS OF CORONARY ARTERY BYPASS GRAFT SURGERY.** RJ Lederman, AC Breuer, MR Hanson, AJ Furlan, FD Loop, DM Cosgrove, FG Estafanous and RL Greenstreet. *Ann Neurol* 1982; 12:297-301.

Among 421 patients undergoing coronary artery bypass graft surgery, 55 (13%) developed 63 new peripheral nervous system (PNS) complications postoperatively. Most common was a brachial radiculoplexopathy, which occurred in 23 patients. Of these, 21 involved lower trunk or medial vein cannulation and the side effected, suggesting that needle trauma played a role. Stretching from chest wall retraction may have caused some cases. Other deficits included 13 saphenous, 8 common peroneal, and 5 ulnar mononeuropathies. Six patients had persistent singultus, suggesting phrenic nerve involvement. Unilateral vocal cord paralysis was found in 5. An isolated partial Horner syndrome and a facial neuropathy were also identified. Hypothermia during surgery was associated with increased risk. Most PNS deficit were transient, and lasting disability was rare.

Herman J. Flax, M.D.

**DIABETIC NEUROPATHY: A CLINICAL, LABORATORY AND ELECTRODIAGNOSTIC STUDY.** EM Halar, RJ Graf, JB Halter, FV Brozovich and TL Soine. *Arch Phys Med Rehabil* 1982; 63:298-303.

The objective of this study was to determine the relationship between nerve conduction velocity (NCV) and hyperglycemia and to assess the extent of NCV changes in adult-onset diabetic patients before and after diabetic treatment. Twenty-five diabetic males (mean age = 50.9 years) were tested twice prior to beginning diabetic treatment. Eighteen of these 25 were also tested at 1, 3, 6, and 12 months after initiation of therapy. Both groups were compared to 23 age-matched controls. The findings revealed that, before treatment, average NCV's of the median, peroneal, sural, and tibial nerves and H-reflex latency results were all significantly impaired. Thus, it appears that the neuropathy in these patients was symmetrical and diffuse. Peroneal and median motor nerves showed the greatest amount of NCV slowing when compared to normal values. Furthermore, median, peroneal, and tibial motor NCV's and H-reflex latencies correlated significantly with the degree of hyperglycemia in diabetic subjects before treatment.

After initiation of diabetic treatment, median motor NCV's after 1, 3, 6 and 12 months showed significant improvement when compared to baseline NCV values (all  $p < 0.05$ ). Also, the improvement in median NCV's after 3 and 12 months and peroneal NCV after 3 months directly correlated to decreased fasting plasma glucose levels ( $p < 0.05$ ).

Herman J. Flax, M.D.

**PERIPHERAL NEUROPATHY AFTER MULTIPLE TETANUS TOXOID INJECTIONS.** L. Reinstein, JM Pargament and JS Goodman. *Arch Phys Med Rehabil* 1982; 63:332-334.

This case documents the 14th reported patient with peripheral neuropathy following tetanus toxoid injection. A 33-year-old man developed profound mixed sensorimotor peripheral neuropathy after receiving 3 tetanus toxoid injections over a 5-month period. Periodic serial electromyographic and nerve conduction studies performed over 2 years suggested both segmental demyelination and axonal neuropathy. The patient experienced partial recovery. Analysis of this case and 13 other reported in literature indicates that in almost all cases (85%) patients had received multiple tetanus toxoid injections. Also, it appears that a prolonged interval of 14 or more days between the tetanus toxoid injection and the onset of neurological symptoms is associated with a poorer prognosis for complete recovery. This is only the second case in the literature documented with nerve conductions.

Herman J. Flax, M.D.

**NUEVOS CRITERIOS DIAGNOSTICOS PARA INFECCIONES DEL TRACTO URINARIO.** Stam W.E., et al. *N. Engl. J. Med.* 307: 463, 1982.

Un estudio de la Escuela de Medicina de la Universidad de Washington ha reevaluado los criterios diagnósticos convencionales para las infecciones del tracto urinario (UTI) en mujeres y ha establecido un nuevo standard. Se encontró que el criterio de mayor o igual a 100 coliformes por milímetro de orina tomada en nuestra intermedia es una prueba diagnóstica

más sensitiva y específica para el manejo de UTI que un conteo de mayor o igual a 100,000 bacterias por milímetro que fue establecido por Kass hace 20 años.

En contraste a los pacientes estudiados por Kass, las 187 mujeres en Washington estaban sintomáticas, pero no tenían pielonefritis ni bacteriuria asintomática. Estudios previos de este grupo demostraron que la mayoría de las mujeres con UTI tienen infecciones agudas del tracto urinario bajo o la vejiga o en ambos y que el síndrome uretral agudo es en realidad una infección coliforme de la vejiga. Estudios anteriores habían demostrado que por lo menos 1/3 parte de las mujeres con una infección coliforme aguda tenían menos de 100,000 bacterias por milímetro de orina tomada a medio chorro.

Para encontrar los nuevos criterios diagnósticos, analizaron muestras de orina primarias (inmediatamente al comenzar a orinar) y muestras a mitad de chorro, además de cultivos rectales y vaginales y muestras de orinas obtenidas por aspiración suprapúbica o sondeos uretrales. Se aislaron coliformes en 98 de las 187 mujeres, por muestras suprapúbicas o de sondeo uretral; 63 con cultivos estériles y 26 con otros organismos aislados. Todas las mujeres con coliformes tenían piuria concomitante, definida por 80 o más células blancas por milímetro de orina. Orinas de medio chorro correlacionaron bien en orinas de vejiga, pero 49% tenía menos de 100,000/ml y 30% menos de 10,000/ml. En el 71% de las orinas de vejiga que estaban estériles, no se encontraron coliformes en muestras a medio chorro.

La presencia de piuria fue una prueba sensitiva, pero no específica. Las muestras a medio chorro fueron altamente sensitivas, pero con una especificidad de 0.71 debido a que cantidades pequeñas de coliformes fueron vistas en algunas mujeres con cultivos de orinas negativas. El criterio tradicional de  $>10^5$  fue 0.99 específico, pero solamente 0.51 sensitivo debido a que las concentraciones de coliformes eran menores en muestras a medio chorro en infecciones por coliformes. El criterio de  $>10^2$  provee especificidad y sensitividad máxima. Utilizándolo como criterio diagnóstico para muestras en pares a medio chorro, 61 de 67 pares fueron consistentes.

Kass ha aceptado que las infecciones pueden estar presentes con menos de  $10^5$  organismos, particularmente si hay uso reciente de antibióticos, ingesta alta de agua, un pH urinario bajo, concentraciones altas de úrea u osmolalidad.

Carlos H. Ramírez-Ronda, M.D.

**STAPHYLOCOCCUS EPIDERMIDIS - DEBE SER CONSIDERADO.** Christensen G.D., et al: Ann. Int. med. 96:1, 1982.

*Staphylococcus epidermidis* ha sido considerada como una bacteria no patógena excepto en casos de heridas, cuando se usan prótesis, o se utilizan puentes cerebrospinales. *S. epidermidis* ha sido aceptado como el causante de la endocarditis en pacientes con enfermedades o reemplazos en las válvulas cardíacas. Ha sido aislado de catéteres intravasculares, pero usualmente descartado como un contaminante o colonizador no patogénico. Este artículo nos hace reevaluar a *S. epidermidis* como un patógeno.

Christensen y asociados hicieron una revisión de 27 casos de septicemia. Once casos indicaban claramente la presencia de *S. epidermidis*; dieciséis casos sólo sugirieron sepsis por este

organismo. Ellos caracterizaron los pacientes clínica y microbiológicamente y analizaron los factores epidemiológicos que podrían estar contribuyendo.

Los 11 pacientes con sepsis por *S. epidermidis* tenían, por lo menos, un catéter intravascular principal en el lugar colonizado por el organismo; el 59% de los cultivos de sangre resultaron positivos para *S. epidermidis*; esto fue demostrado en más de uno de los cultivos utilizando biotipo con fago o antibiograma. Las fuentes para sepsis fueron los catéteres intravasculares que permanecieron en el interior por largos períodos de tiempo y los que se utilizaron para hiperalimentación. Dos de los once pacientes, que presentaron fiebre de una o más semanas de duración, eventualmente murieron de sepsis.

Los 16 pacientes en que se sospechaba sepsis por *S. epidermidis* presentaron cuadros clínicos menos severos, con fiebre baja y de menor duración. Estos pacientes también estaban en tratamiento endovenoso. Hubo crecimiento de *S. epidermidis* en solo 50% de los catéteres, y solo 20% de los cultivos de sangre resultaron positivos. Dos pacientes de este grupo aparentemente murieron de sepsis. Se hicieron autopsias de 3 de los 4 casos de muerte y se demostró la formación de abscesos y pulmonía por *S. epidermidis*.

Epidemiológicamente, se asociaron los casos con la higiene en las técnicas médicas y de las enfermeras y con el cuidado de los catéteres. Cultivos de las manos y nariz demostraron una alta razón de portadores de *S. epidermidis* en un número significativo del personal. Los microorganismos que se aislaron de la sangre de pacientes y de catéteres eran, en su mayoría resistentes a antibióticos, a diferencia de los que se aislaron de áreas de la piel escogidas al azar. Estos microorganismos resistentes eran del mismo tipo de los que se encontraron de los médicos y enfermeras. Comparando con *S. epidermidis* aislados de cultivos de piel, más de la mitad de los aislados en pacientes sépticos eran resistentes. Los patrones de resistencia a antibióticos eran extremadamente variables, pero la resistencia a clindamicina, tetraciclina, cloramfenicol, penicilina y ampicilina era frecuente.

C.H. Ramírez-Ronda, M.D.

**SINDROME DEL NODO ENFERMO EN NIÑOS Y ADOLESCENTES COMO UNICA MANIFESTACION CARDIACA O ASOCIADO A CARDIOPATIAS CONGENITAS NO-OPERADAS.** Beder SD, Gillette PC, Garson A, Porter C, McNamara D. Am J Cardiol 1983; 51:1133-36.

El síndrome del nodo enfermo (SSS) es de aparición poco frecuente en niños no expuestos a cirugía cardíaca. Los autores revisan la experiencia de 9 años en el Hospital de Niños de Texas en 11 pacientes con SSS no quirúrgico. Se revisó la clínica, los electrocardiogramas (ECG) y la data electrofisiológica de estos pacientes. Hubo síncope en 5 pacientes y bradicardia en 9.

Basados en su experiencia los autores señalan la bradicardia sinusal en ECG en reposo o ambulatorios como el indicador más efectivo de anomalía del nodo sinusal. El síncope, las palpitaciones y el dolor precordial también están casi siempre presentes. Electrofisiológicamente se encontró que el tiempo de recuperación del nodo sinusal estaba frecuentemente prolongado (6 casos). El período refractario atrial también suele



prolongarse y el tiempo de conducción seno-atrial se consideró un indicador poco sensitivo de la función sinusal.

En este grupo de pacientes con SSS no quirúrgico se encontró una incidencia mayor de enfermedad del músculo atrial y nodo atrioventricular que en su serie de SSS post procedimiento de Mustard.

Los autores recomiendan que todo paciente con síntomas o hallazgo en ECG que sugiera disfunción sinoatrial debe estudiarse electrofisiológicamente. La selección adecuada del tratamiento, ya bien sea con fármacos antiarrítmicos o marcapasos dependerá de un análisis minucioso de todos los componentes del sistema de conducción cardíaco en pacientes con SSS.

Rafael Villavicencio, M.D.

**EFFICACY OF HEPATITIS B IMMUNE GLOBULIN FOR PREVENTION OF PERINATAL TRANSMISSION OF THE HEPATITIS B VIRUS CARRIER. FINAL REPORT OF A RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL. Beasley RP, Hwang L-Y, Stevens CE, et al, Hepatology 1983; 3: 135-141.**

Cerca de un 90% de los neonatos de madres portadoras del virus de hepatitis B y del antígeno e (HBeAg) desarrollan infección crónica de hepatitis B. Muchos de los neonatos permanecen portadores del virus por vida y muchos de estos desarrollan hepatitis crónica, cirrosis, y con frecuencia cáncer hepatocelular. Los autores reportan los resultados de un estudio controlado y randomizado empezado en 1978 y terminado en el 1982 donde recién nacidos de madres portadoras crónicas del virus de hepatitis B y del antígeno e se randomizaron a recibir placebo, una inyección de inmunoglobulina contra hepatitis B (HBIG) al nacer, o HBIG al nacer y a los 3 o 6 meses. Al cabo de 15 meses de nacidos la frecuencia de portación del virus de hepatitis B fue: 92% en el grupo placebo, 54% en el grupo que recibió una dosis y 26% en el grupo que recibió tres dosis. Como los títulos de anticuerpo contra el virus de hepatitis B desaparecen con el tiempo (a menos que ocurra inmunización pasiva-activa) los autores recomiendan el uso de la vacuna de hepatitis B en adición a HBIG en estos niños.

Angel Olazábal, MD

**RANDOMIZED COMPARATIVE STUDY OF THE EFFICACY FUROSEMIDE VERSUS SPIRINOLACTONE IN MONAZOTEMIC CIRRHOSIS WITH ASCITES. Pérez-Ayuso, RM, Arroyo, V., Planas R, et al. Gastroenterology 1983; 84:961-968.**

Los autores comparan la eficacia de furosemida y de spirinolactona en 40 pacientes con cirrosis y ascitis y que no tenían azotemia. Las dosis iniciales fueron de 80 mg y de 150 mg por día de furosemida y de spirinolactona. Si no respondían se daba una segunda dosis diariamente. Algunos de los resultados sobresalientes fueron:

1. la respuesta de diuresis fue mejor con spirinolactona;
2. la mayoría de los que no respondieron con furosemida tuvieron diuresis cuando se cambiaron a spirinolactona;
3. La respuesta de los diuréticos se relacionó con la actividad del sistema renina-aldosterona (peor respuesta en los que tenían la actividad aumentada).

Angel Olazábal, MD

**CRITERIOS DE SELECCION PARA EL OXIGENO A LARGO PLAZO (EDITORIAL). Petty T. Am Rev Resp Dis 127(4): 397, 1983.**

El oxígeno a largo plazo en el hogar es un tratamiento ya establecido en el cuidado de pacientes seleccionados de enfermedad crónica obstructiva pulmonar con hipoxemia.

Los beneficios de su uso incluyen: aumento en la supervivencia, reducción en hospitalizaciones, mejoramiento en la tolerancia al ejercicio y mejor calidad de vida. Las diversas formas ahora disponibles para el uso de oxígeno en el hogar hacen que su uso haya aumentado y esté disponible en todas las áreas de Estados Unidos y en Puerto Rico, pero no todos los pacientes con enfermedad crónica obstructiva pulmonar (ECOP) requieren o se benefician del oxígeno en el hogar. Las desventajas entre otras cosas son el costo, lo inconveniente y las cargas sociales y emocionales que rodean el uso de oxígeno en el hogar.

Es bien importante el desarrollar criterios por los cuales los médicos puedan juzgar cual de sus pacientes son verdaderos candidatos a esta modalidad terapéutica.

Un artículo en el mismo número señala como criterio, la baja en la presión arterial pulmonar media al descanso de más de 5 mm Hg y como índice de mejor supervivencia en dos años que los que no tuvieron esa mejoría.

Esto no quiere decir que se tiene que hacer un cateterismo cardíaco ni estudios en ejercicio para recetar oxígeno en el hogar pero sí que se necesita criterios clínicos aplicados críticamente para seleccionar esos pacientes.

Como sugerencias el autor recomienda someter al paciente a un régimen de tratamiento completo con broncodilatadores, antibióticos, diuréticos y a veces esteroides para obtener la mejoría máxima posible antes de concluir que la hipoxemia no puede ser mejorada.

Cuales deben de ser las bases o criterios a seguirse:

1) Sintomatología, el paciente debe de tener ECOP severa y estar sintomático.

2) Espirometría y gases arteriales, cuando el paciente esté libre de una exacerbación de su enfermedad. Preferiblemente luego de tres semanas de tratamiento intenso volver a estudiarle y si entonces tiene una tensión de oxígeno arterial de 55 mm Hg o menos es candidato a oxígeno prolongado.

3) Otros criterios clínicos de gravedad como: evidencia de hipertensión pulmonar por ECG, evidencia radiológica o por examen físico.

4) Hay pacientes que con oxígeno más alto de 55 mm Hg son buenos candidatos si la tensión de oxígeno baja significativamente durante el sueño si tiene eritrocitosis sin causa aparente (que no sea Policitemia vera) o si tiene cambios mentales que sugieren hipoxemia cerebral.

Si se siguen estos criterios es posible que uno haga factible el que pacientes que puedan beneficiarse se beneficien y se puedan evitar esperanzas falsas, molestias y gastos innecesarios a pacientes que no van a beneficiarse de ellos.

**Nota editorial:** En nuestra experiencia el número de pacientes que reúnen estos criterios es pequeño y tanto en Puerto Rico como en los EE.UU. el número de pacientes usando alguna modalidad de oxígeno en el hogar es cada día mayor no teniendo la mayoría de ellos verdadera indicación.

Ramón E. Figueroa Lebrón, MD, FCCP

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# Medicolegal Decisions



## HOSPITAL AND PHYSICIANS LIABLE FOR PATIENT'S RETROLENTAL FIBROPLASIA

A hospital and physicians were liable for permitting an infant patient to be exposed to increased oxygen for a prolonged period, even though it was a common practice at the time, a New York appellate court ruled.

The patient was born in July 1953 five to six weeks' premature and weighing 1,362 gm. He was transferred to the hospital designated by the city as a premature nursery care center. A pediatric resident found the infant to be in good condition and had him placed in an incubator with oxygen at 3-4 liters. The resident knew that oxygen had been implicated as a cause of retrolental fibroplasia (RLF). He therefore ordered that oxygen be reduced as tolerated. According to hospital records, the nurses reduced the oxygen flow to 2.5 liters and the concentration from 35 to 30 percent.

Two days later, a physician on the hospital staff ordered the oxygen concentration increased, based on a random allocation of babies into one of two groups for monitoring as part of a study. She countermanded the resident's orders without examining the patient or speaking to the infant's parents.

Over a period of 28 days, the oxygen was increased a high of 9 liters, from 30 percent to a high of 82 per cent. On two or three occasions during the high-oxygen state, ophthalmoscopic examination showed the infant's optical media to be hazy. When the infant was removed from the high-oxygen environment, a large hemorrhage was found in the right eye, with dilation and distortion of the blood vessels. A week later, there were hemorrhages, swelling, and collection of fluid in both eyes. On discharge, swelling totally enveloped the eyes.

In 1975, the patient sued the hospital the resident, and the physician who ordered the oxygen increased, alleging malpractice and failure to obtain informed consent from the parents before increasing the oxygen. The man was almost totally blind and suffered daily from pain and irritation. His eyes were shrinking and they would have to be enucleated and replaced with plastic ones. The jury found that the resident was not liable for malpractice but was liable for failure to obtain informed consent. The other physician and the hospital were found liable under both theories.

On appeal, the court said that prolonged exposure to oxygen had been recognized as the leading cause of RLF since 1954. Although the patient's treatment in 1953 was in accordance with community standards, the court found that both the hospital and the second physician were aware of the dangers of excess oxygen and knew or should have known that the infant was progressing well in a lower oxygen environment. The court said that the jury could have found that the hospital should have removed the infant from the high-oxygen environment long before it did because of the results of the ophthalmoscopic examinations. The court found that the resident should not have been found liable at all but that the second physician and the hospital failed in their duty to the patient and that the verdict of liability against them should stand.—*Burton v. Brooklyn Doctors Hospital*, 452 N.Y.S.2d 875 (N.Y.Sup.Ct., App.Div., July 22, 1982)

## NEW TRIAL FOR SUIT AGAINST OBSTETRICIAN

A physician was entitled to a new trial of a malpractice claim against him because of faulty jury instructions by the trial court, a New York appellate court ruled.

A 23-year-old claimant sought damages for having been born with cerebral palsy, allegedly as a result of malpractice during his delivery by cesarean section. He filed suit against his mother's obstetrician, a second physician, and the hospital. He presented several different theories of alleged malpractice, some based solely on the physician's acts and others relating to the responsibilities of the hospital.

Despite the complexity of the trial and contrary to the requests of the parties, the trial court gave the jury only general malpractice instructions. The court did not explain to the jury the various theories of liability as they related to the physician and the hospital and did not indicate the acts for which each party would be liable. The jury returned a verdict against the obstetrician and in favor of the hospital and the second physician.

On appeal, the court reversed the decision. The court said it was impossible to determine whether the verdict against the physician was properly based. The court noted that at least two of the theories of liability were not applicable to the physician. Oxygen deprivation to the fetus could have been caused by shock after administration of the spinal anesthetic by the anesthetist, the court said. It could also have occurred during efforts to resuscitate the cyanotic newborn.

Since it was unknown whether the verdict was based on acts for which the physician was liable, a new trial was necessary, the court said.—*Caputo v. Frankel*, 452 N.Y.S.2d 649 (N.Y.Sup.Ct., App.Div., July 19, 1982)

## FOREIGN MEDICAL SCHOOL LIABLE TO STUDENT

A student was entitled to damages for misrepresentations in a foreign medical school's bulletin that were material to his decision to attend the school, a federal trial court in New York ruled.

The student was employed as a hospital laboratory technician when he saw an advertisement of the school, which was located in the West Indies. He sent for a bulletin and admissions material.

The student resigned from his job and enrolled in the school. When he allegedly discovered that the course of study, faculty, and facilities had been falsely described in the bulletin, he withdrew from the school. Pursuant to its stated policy in the bulletin, the school refused to refund his tuition.

The student was unable to obtain a position with his former employer and finally found a job at a lower salary. In a suit against the school, he sought compensatory damages for tuition and fees, his round trip air fare, and lost wages.

The student contended that the school had falsely represented in its bulletin that it had 1) a library with periodicals, books, and audiovisual aids; 2) laboratory facilities that included microscopes, microscopic slides, and skeletons; and 3) a set of prepared slides and a microscope for the histology class. The bulletin contained a photograph of a hospital which the student claimed was calculated to give the impression that the students could use its facilities when, in fact, they could not. It also indicated that classes would start in May, when actually only two classes started then and the remainder in June. Finally, the number of faculty members was less than one-half the number given in the bulletin, one class actually being taught by a student enrolled in the school.

The court found that the student proved by clear and convincing evidence that the school materially misrepresented its facilities and faculty and that his testimony that he relied on the statement in the bulletin was credible. The school president contended that the information in the bulletin was accurate when it was prepared. The court found that the school had a duty to inform students of major changes that could affect their decision to attend the school.

Since the measure of damages in an action for fraud is the actual pecuniary loss, the court awarded damages only for tuition, fees, and air fare. The court said that lost wages were not shown to be proximately caused by the school's conduct and that punitive damages were not appropriate where the conduct complained of did not affect the public generally or involve a gross departure from moral behavior. —*Idrees v. American University of the Caribbean*, 546 F.Supp. 1342 (D.C., N.Y., Sept. 17, 1982)

## SUIT FOR ALLEGED IMPROPER READING OF X-RAY BARRED BY STATUTE OF LIMITATIONS

A malpractice action for alleged negligence in misreading an X-ray was barred by the statute of limitations, a Georgia appellate court ruled.

A patient had an employment-related accident and was X-rayed on September 30, 1975. The physician allegedly did not observe or alert the patient to an abdominal aortal aneurysm, which was revealed by the X-ray. On February 2, 1977, the patient collapsed and died two days later from rupture of the aneurysm. On January 31, 1979, the widow filed complaints alleging wrongful death and pain and suffering from the physician's alleged negligence. A trial court granted summary judgment for the physician on the ground that the statute of limitations barred the actions.

On appeal, the appellate court reversed. The trial court again granted summary judgment, and the widow filed a second appeal. Affirming the trial court's judgment, the appellate court acknowledged that it had made an erroneous interpretation of an amendment to the statute of limitations in its first opinion. While the case was awaiting trial after the first appeal, the state Supreme Court, in another case, had repudiated the appellate court's reasoning.

The appellate court said that the applicable statute of limitations began to run on the date the alleged malpractice occurred. Since the actions were filed more than two years later, they were barred, the court said. —*Hart v. Eldridge*, 293 S.E.2d 550 (Ga.Ct. of App., July 16, 1982).

## X-RAY TECHNICIAN SHOULD NOT HAVE BEEN TERMINATED BY HOSPITAL FOR PREGNANCY

A hospital's possible liability for X-ray exposure to a pregnant technician did not provide a "business necessity" for terminating the employment of the technician, a federal trial court in Alabama ruled.

The technician was hired by the hospital in August 1980. In October, her physician confirmed her pregnancy. He said that she should be able to work until about April 1981, if she followed the safety precautions generally prescribed for X-ray technicians. Shortly after the director of radiology and the chief radiologist learned of the pregnancy, the technician's employment was terminated. Testimony later revealed that the only reason for the termination was the pregnancy.

The technician sued the hospital, claiming violations of the Civil Rights Act. The hospital contended that termination of the technician's employment was a business necessity and that nonpregnancy was a bona fide occupational qualification for operation of its enterprise.

The court found that the technician's pregnancy did not undermine her ability to take X-rays of patients. Even if the concept of a purpose of safe and efficient operation of the business was extended to include avoidance of possible litigation and potential liability of the fetus, the court said, the hospital did not meet the requirement of the business necessity defense that there were no acceptable alternatives.

Evidence revealed that, prior to the technician's termination, two pregnant white radiology technicians were not fired but that greater precautions were taken and one was allowed to read X-ray films during her pregnancy. The court found that the hospital failed to show that no alternatives to its discriminatory treatment of the technician were available.



As to the bona fide occupational qualification defense, the court said that the hospital must show a connection between pregnancy risks and impaired ability to perform the job. The court found that pregnancy would not have affected the technician's performance as a radiologist and, therefore, the hospital could not rely on that defense.

The court held that the hospital's abrupt termination of the technician's employment constituted a violation of the Civil Rights Act and awarded her \$7,361.76 as damages. — *Hayes v. Shelby Memorial Hospital*, 546 F.Supp. 259 (C.C., Ala., Aug. 18, 1982)

### PATIENT WHOSE BABY DIED AWARDED \$40,000 DAMAGES

Negligence by a general practitioner who assumed another physician's responsibility for care of a pregnant patient was causally connected with her infant's death, a Louisiana appellate court ruled.

The patient first learned that her physician was on vacation when she called after labor pains started. She was admitted to the hospital, and a call was made to the answering service of the general practitioner, who was taking his calls.

The physician called the hospital three times in six hours, but did not request an examination. Only a nurse was in attendance when delivery occurred, and the physician arrived 15 minutes later. Tests that would have indicated that the baby was in distress after birth were ignored, except for an effort at resuscitation and giving the baby oxygen. The infant died two hours after birth.

The patient sued her own physician, the general practitioner, and the hospital. The trial court dismissed the suit, finding that the patient did not prove by a preponderance of evidence that either the physician or the hospital behaved contrary to the community standard of care.

On appeal, the court said that the patient's physician was remiss in failing to notify her that he would be absent, but found no evidence connecting him with the treatment administered by the general practitioner or the hospital. The court also found no negligence on the part of the hospital.

As to the general practitioner, the court found no explanation as to why he failed to go to the hospital during the 6 hours after he was called. At the trial, there was conflicting testimony by medical experts as to whether the infant could have been saved and as to whether there were indications that the infant was in danger and special treatment should have been administered.

The general practitioner, who had no specialized training in obstetrics, assumed responsibility for care of the patient without any medical history or records. Considering all the circumstances, the appellate court found that there was ample evidence that he did not exercise ordinary skill employed under similar circumstances by other members of his profession. The court found that he failed to use reasonable care, diligence, or his best judgment and that his negligence was causally connected to the infant's death. The patient was awarded \$40,000. — *Moran v. Dean*, 416 So.2d 351 (La.Ct. of App., June 8, 1982)

### ORTHOPEDIST NOT NEGLIGENT IN SURGERY ON PATIENT'S LEG

A trial judge properly refused to instruct a jury on the doctrine of *res ipsa loquitur* where there was insufficient evidence to establish that negligence was the most plausible explanation for nerve damage, a Louisiana appellate court ruled.

A 42-year-old man consulted his family physician because of a left knee injury. The physician referred him to an orthopedic surgeon. When the surgeon's treatment did not help, the physician referred him to a second orthopedic surgeon.

The second surgeon performed an operation on the leg, thinking that some kind of growth might be pressing on the peroneal nerve. He found no tumor but decided that a band of tissue was compressing the nerve and performed an internal neurolysis.

After the operation, the patient was unable to lift his left foot. A neurosurgeon examined him and concluded that he had a nerve palsy. He operated on the patient and found that the peroneal nerve was injured but not severed and was regenerating itself.

The patient sued the second orthopedic surgeon, alleging malpractice. The trial court decided for the surgeon.

On appeal, the patient contended that circumstantial evidence suggested that negligence by the surgeon was the most plausible explanation of the nerve damage and that the trial judge erred in refusing to charge the jury on the doctrine of *res ipsa loquitur*. The appellate court said that medical witnesses at the trial generally agreed that the surgeon's manipulation of the previously injured nerve during the operation contributed to the nerve paralysis and resulting drop foot. The neurosurgeon pointed out, however, that it would have been impossible to perform an operation of this type without manipulating the nerve. He found nothing during the course of his operation that indicated any improper surgery by the orthopedic surgeon. There was no evidence that the nerve had been severed.

An orthopedic surgeon testified that internal neurolysis was the proper procedure when an operating surgeon found that a peroneal nerve was flattened because of external pressure. He concluded that the examination, diagnosis, and treatment given by the surgeon complied with the standard of care. The orthopedic surgeon who first treated the man also failed to find any negligence on the part of the surgeon. A medical review panel concluded that he did not fail to meet the standard of care.

On the basis of the record, the appellate court found that the surgeon effectively rebutted any inference of negligence. — *Rogers v. Brown*, 416 So.2d 624 (La.Ct. of App., June 15, 1982; rehearing denied, July 23, 1982)

### NEW TRIAL FOR FRACTURE PATIENT'S MALPRACTICE SUIT

A trial court erred in submitting an issue of contributory negligence to a jury in a malpractice action, a North Carolina appellate court ruled.

A patient consulted a physician when her arm was fractured in an automobile accident. He performed a closed reduction and told her to return in a week. X-rays taken after the reduction showed a 50 to 60 percent apposition fracture fragment. During the next 3 1/2 months, the patient kept all her appointments with the physician. The degree of apposition at the fracture site decreased to 10 percent by the end of 2 1/2 months, but the physician did not inform the patient.

About 2 1/2 months after her last appointment with the physician, the patient consulted an orthopedic surgeon. He had her admitted to a hospital and performed an open reduction of the fracture.

The patient brought a malpractice action against the physician, contending that he negligently performed a closed reduction of the fracture, which resulted in non-union, and that she ultimately had to consult an orthopedic surgeon. She alleged that she experienced pain and suffering, a permanent partial disability, and a permanent deformity in that her injured arm was shorter than her other arm.

At the trial, the orthopedic surgeon testified that the physician had ample opportunity to observe the healing process of the arm. Another physician testified that if the physician told the patient that she was healed and capable of any type of

work his conduct would constitute a deviation from the standard of care.

The physician being sued testified that the patient's fracture did not heal properly within the normal period and that he was greatly concerned about the progressive increase in angulation at the fracture site. He also said that he had a duty to advise of the possibility of an adverse result but did not so inform the patient because he did not want to upset her. The jury found that the patient was injured by the physician's negligence and that she contributed to her injuries by her own negligence. The jury awarded the patient \$20,500.

On appeal, the court upheld the trial court's denial of a directed verdict for the physician, considering the fact that the physician made no effort to refer the patient to a specialist. As to the submission of an issue of contribution to the jury, the court found that where the damages sought were based on the physician's alleged negligence prior to her last appointment with him, there was no evidence that the degree of deformity of the patient's arm would have been decreased or increased by anything she did during that period. The court vacated the trial court's judgment and sent the case back for a new trial. —*Powell v. Shull*, 293 S.E.2d 259 (N.C.Ct. of Ap., July 6, 1982)

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By making your fresh start without cigarettes, you are giving your child a Head Start to life: good health at birth. This is the kind of Head Start you can give your child\*\*:

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\* From an Australian Heart Foundation pamphlet.

\*\* Information taken from the US Surgeon General's report: Smoking and Health, 1979.

\*\*\* British Medical Journal, 11th August 1979.



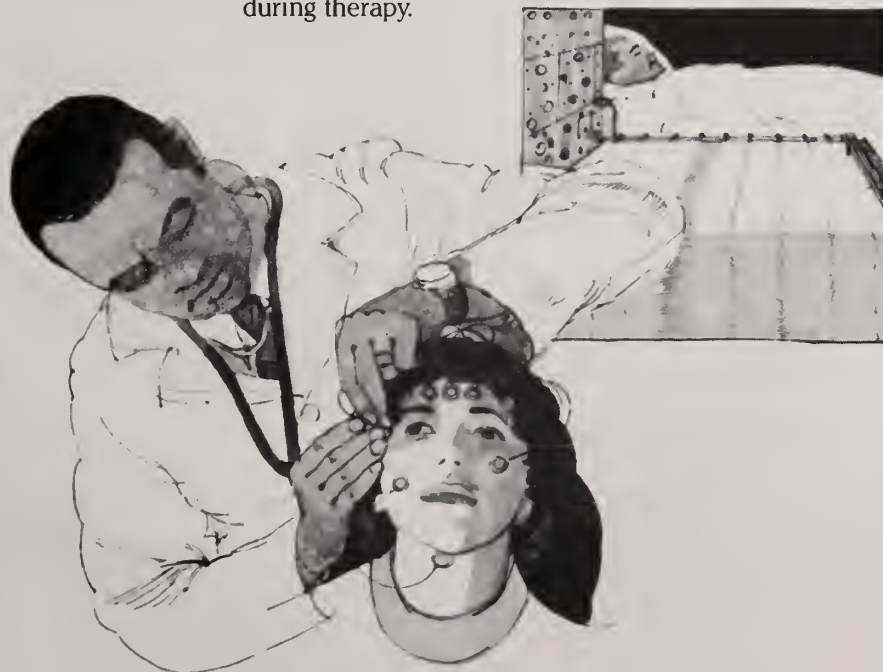
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## flurazepam HCl/Roche

### 15-mg/30-mg capsules



- Studied extensively in the sleep laboratory—the most valid environment for measuring hypnotic efficacy.<sup>1-12</sup>
- Studied in over 200 clinical trials involving over 10,000 patients.<sup>13</sup>
- During long-term therapy, which is seldom required, periodic blood, kidney and liver function tests should be performed.
- Contraindicated in patients who are pregnant or hypersensitive to flurazepam.
- Caution patients about drinking alcohol, driving or operating hazardous machinery during therapy.



**References:** 1. Kales A et al: *J Clin Pharmacol* 17:207-213, Apr 1977 and data on file, Hoffmann-La Roche Inc., Nutley, NJ. 2. Kales A: Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 3. Zimmerman AM: *Curr Ther Res* 13:18-22, Jan 1971. 4. Kales A et al: *JAMA* 241:1692-1695, Apr 20, 1979. 5. Kales A, Scharf MB, Kales JD: *Science* 201:1039-1041, Sep 15, 1978. 6. Kales A et al: *Clin Pharmacol Ther* 19:576-583, May 1976. 7. Kales A, Kales JD: *Pharmacol Physicians* 4:1-6, Sep 1970. 8. Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc* 27:541-546, Dec 1979. 9. Dement WC et al: *Behav Med* 5:25-31, Oct 1978. 10. Vogel GW: Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 11. Karacan I, Williams RL, Smith JR: The

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**Dalmane®<sup>IV</sup>**  
(flurazepam HCl/Roche)

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

**Contraindications:** Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patient to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

**Precautions:** In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

**Adverse Reactions:** Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, e.g., excitement, stimulation and hyperactivity.

**Dosage:** Individualize for maximum beneficial effect. **Adults:** 30 mg usual dosage; 15 mg may suffice in some patients. **Elderly or debilitated patients:** 15 mg recommended initially until response is determined.

**Supplied:** Capsules containing 15 mg or 30 mg flurazepam HCl.

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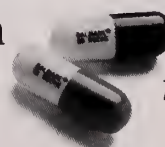
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